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BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

SATURDAY NOVEMBER 20 1948

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 20 1948

THE PHYSIOLOGICAL BASIS OF NEUROMUSCULAR DISORDERS*

BY

Sir HENRY DALE, O.M., G.B.E., F.R.C.P., F.R.S.

To-day's discussion is to deal with the bearing of recent physiological observations, and of the interpretations which have been applied to them, on clinical studies of neuromuscular disorders. The choice of myself as opener, and of subjects by those who are to follow me as invited contributors, would appear to direct our discussion chiefly to the clinical applications of the large and growing body of evidence for the transmission of effects from the endings of nerve fibres to contiguous responsive cells by the liberation of chemical transmitters.

Chemical Transmission at the Periphery

We may take for granted, as generally accepted, that the effects of impulses in the efferent post-ganglionic fibres of the autonomic nervous system are so transmitted to involuntary muscle and gland cells by the liberation of one of two known transmitters—adrenaline (sympathin) and acetylcholine. In this case the nature of the transmitter determines also whether the effect produced by the arrival of nerve impulses at the endings will be augmentation or inhibition of a spontaneous activity; and the two transmitters commonly produce opposite effects on the same layer of involuntary muscle. How they do so is one of the fundamental problems of pharmacology; but we might note in passing that it does not seem to have any intelligible relation to the hypothesis, which we shall meet later, according to which conduction of excitation along nerve fibres, and from their endings to receptive cells, is one uniform and electrically conducted process, everywhere due to the depolarizing effect of liberated acetylcholine.

For the purpose of the discussion I think that it must be said that these phenomena of chemical transmission from peripheral involuntary nerve endings, though we have been considering them as theoretical possibilities for nearly 45 years and have known them as well-established experimental facts for more than 25 years, have had relatively little influence on the understanding of clinical conditions. Their main effect on clinical practice has been, I think, to clarify understanding of the actions of well-known medicinal agents such as atropine, physostigmine, adrenaline itself, and the ergot alkaloids, and to guide the search for new ones such as carbachol, prostigmin, the fluorophosphonates and simpler organic phosphates, ephedrine, and others. It may be, however, that the application of this more intimate knowledge concerning the mechanism of the control of such involuntary functions has not yet been exploited to its full value in clinical medicine.

I suspect that it may have been largely forgotten by now that Otto Loewi, many years before his epoch-making experiments on chemical transmission, had described in Graves's disease a supersensitiveness of involuntary muscle to adrenaline of such a kind that the mere instillation of it into the conjunctival sac of the patient produced abnormally a dilatation of the pupil. I wonder whether there may not be other abnormal reactions of involuntary muscle to the transmitters or their analogues yet to be discovered which might be useful in diagnosis or indicative of aetiology. I know, of course, that there has been a voluminous literature on what were called the "vagotonic" and the "sympathicotonic" diatheses; and I am not unaware of the perils to which a sprightly imagination may expose its owner when given the freedom of such clinical borderlands. I only raise the question, then, whether the positive knowledge and the specific reagents which we now possess might not be used to commit some of such conceptions to the crucible of experiment, and to enable us perhaps, with the refined product, to approach nearer to the ideal of that stimulating sceptic among my clinical teachers the late Mr. Barrett Lockwood, who used to offer to believe in a diathesis when one of his physician colleagues could show it to him "on a plate."

Before leaving the transmission of nervous effects at the periphery to involuntary effectors we ought to take note of the suggestion that histamine may act as a third transmitter. The evidence, not yet by any means so definite as for the two already mentioned, indicates that histamine may be released by the so-called "antidromic" nerve impulses at the endings of those terminal nerve branches which supply the networks of minute blood vessels to the skin.

Transmission at Ganglionic and Nerve-to-end-plate Synapses

I have no doubt that to-day's discussion will centre mainly on the interpretation of various defects of nervous and muscular function in the light of the evidence obtained in more recent years for a chemical transmission of the excitatory process from the endings of motor-nerve fibres to the motor end-plates of voluntary muscles, from the endings of preganglionic nerve fibres to the nerve-cells of autonomic ganglia, and perhaps at certain comparable synaptic junctions in the central nervous system. In all the cases concerning which we have clear evidence so far the

*Read in opening a discussion in the Section of Physiology at the Annual Meeting of the British Medical Association, Cambridge, 1948.

transmitter is acetylcholine; and the actions of that substance on the motor end-plates and on the autonomic ganglion cells are those which are grouped together as its nicotine actions, because these structures are sensitive to acetylcholine after atropine has annulled its peripheral effects on the involuntary effectors and are, on the other hand, made insensitive to acetylcholine by excess of nicotine, by curarine, or, as we must bear in mind, by a persistent excess of acetylcholine itself.

Before we consider particular clinical abnormalities in relation to this conception we ought to have a clear idea of what it involves, and to note that it cannot yet be regarded as accepted by all who concern themselves with such matters. In the form in which my colleagues and I have advocated it the theory postulates chemical transmission at motor myoneural and ganglionic synapses as a process essentially different from that by which the excitatory process is conducted along either a nerve or a muscle fibre in continuity. It is incompatible, accordingly, with the facts that the excitatory transmission is irreciprocal only at these junctions and that it is blocked only at these by poisons such as curare or modified by such as physostigmine, contrasting sharply in these respects with conduction along continuous fibres, which goes equally well in both directions and is not elicited, stopped, or in any way modified by acetylcholine itself or by the alkaloids mentioned in concentrations even much greater than those which are so effective at the synapses. It may be said, further, that our conception restricts the transmitter function of acetylcholine to the sites where nervous impulses demonstrably liberate it, where it can be shown to act in the manner required, and where its action is annulled or modified by agents which comparably alter the effects of nerve impulses incident there.

We are content, while others seek further evidence, to accept the prevailing view of the momentary process of excitation at a point on a nerve or muscle fibre as due to a biochemical change, possibly the mobilization and reattachment of potassium ions, entailing a momentary loss or reversal of a resting surface-potential at each successive point as the process is conducted in either direction along the fibre by the successive closure of local electrical circuits. When this electrically conducted process reaches the ending of the nerve fibre we suppose that it releases a tiny charge of acetylcholine which during its momentary persistence causes an excitatory depolarization at the surface of ganglion cell or motor end-plate, presumably by a mobilization there of potassium ions, and that the process of excitation is then, as before, electrically propagated along the post-ganglionic nerve fibre or the muscle fibre. It is demonstrable by experiment that when ganglion cells or motor end-plates are treated with curarine they no longer respond to application of acetylcholine or to nerve impulses incident at the synaptic endings but still respond normally to the application of a potassium salt.

This conception, as I said, has not yet won general acceptance. There are those who find it difficult to resign the idea that electrical conduction will suffice to get the excitation across the junctions as well as along the continuous fibres; but they appear thus to become involved in complicated subsidiary hypotheses to account for the special character of transmission at the synapses and for the appearance there, on arrival of nerve impulses, of acetylcholine in a concentration adequate to excite ganglion cells or end-plates. Others, in particular Dr. Nachmansohn, have also tried to eliminate the special character of synaptic transmission by supposing that the release and disappearance of acetylcholine provide also the mechanism for the excitatory depolarization at each successive point on nerve and muscle fibre. They wish to have excitation everywhere cholinergic and everywhere electrically conducted. There is a kind of attraction, especially for some minds, in such comprehensive master-key conceptions. But the proponents of this one have also the formidable task of upholding it against most of the direct evidence. Nobody has been able to show that acetylcholine excites nerve fibres: according to the most recent evidence they are as indifferent to it as to cane-sugar; while its excitation of effector and nerve cells first brought it to notice and has become a physiological commonplace. Even the fact that acetylcholine and the enzymes concerned with its formation and destruction are to be found along the course of nerve fibres and are not wholly concentrated at their endings applies only to cholinergic fibres, whereas others conduct impulses by a process not perceptibly different.

I think that it can also be claimed that this theory of the intervention of a special pharmacodynamic phase in the transmission of the excitatory process at these peripheral synapses, and especially from motor-nerve endings to muscle end-plates, has already contributed to a better understanding of certain neuromuscular disorders than any which could be offered by the older theory of a uniform electrical mechanism of conduction along fibres and across synapses. On the latter basis we could only discuss whether a particular anomaly was due to abnormal function of nerve or of muscle, and it offered no special explanation for defects at the synapse when excitability and conductivity of both nerve and muscle were normal. There are, of course, conditions affecting nerve fibres or muscle fibres as a whole—the neuritis caused by diphtheria toxin or by other poisons, the nerve degeneration and muscular atrophy following the attack of the poliomyelitis virus on anterior horn cells, or other so-called muscular dystrophies. None of these, however, are our concern. It is the functional defects or anomalies affecting transmission from motor nerve to muscle without anomaly of conduction in the fibres of nerve or muscle on which the evidence for a chemical mechanism at the junction throws light. Such anomalies may be produced by vegetable alkaloids or bacterial toxins, or by morbid conditions of obscure aetiology.

Action of Some Poisons

Perhaps the way in which the chemical theory can add detail and give a specific character to knowledge concerning transmission at a synapse can be most easily presented by considering first the actions of certain poisons. Since Claude Bernard we have known that curare blocks transmission from motor-nerve ending to muscle end-plate, leaving both nerve and muscle fibre normally excitable and conductile. On the electrical theory of synaptic transmission we could go no further; curare might stop conduction in the naked nerve terminals or make the end-plate inexcitable. Now we know by specific experiments, including those made by Buchthal with minute direct applications to the isolated unit, that curarine blocks the effect on the end-plate not only of an impulse reaching the nerve ending but also, and simultaneously, of the application of a minute quantity of acetylcholine, but leaves the same end-plate normally responsive to direct electrical stimulation and to the application of a small dose of potassium chloride. This enables us to conclude that the effect of curarine is to make the muscle end-plate specifically insensitive to acetylcholine and the same can be shown to hold for the ganglion cell when curarine is appropriately applied to it. At the same time it makes clear the danger of applying such terms as "curarizing" or "curare-like" loosely to any action which interrupts or weakens transmission from motor nerve to voluntary muscle. There are obviously several ways in

which superficially similar effects of this kind could be brought about: paralysis of conduction in the naked terminal nerve branches; failure of the adequate liberation of acetylcholine from their actual endings either because the depots normally holding it ready there for release are not adequately replenished or because, though full, they do not yield their store when a nerve impulse reaches them; and excess of cholinesterase in such relation to the depots that acetylcholine, though normally released, is destroyed too quickly to produce its full effect. All these should, if possible, be eliminated by experiment before an action is described as "curare-like." An example has recently been provided by the action of the extremely potent toxin of *Bacillus botulinus*. This interrupts the transmission and leaves both nerve and muscle normally excitable, like curarine; but experimental analysis in greater detail has shown that the muscle end-plates remain normally responsive to acetylcholine and that it is the release of acetylcholine by nerve impulses which fails. The action is on the nervous side of the synapse, but whether on conductivity in the ultimate branches of the nerve fibres or on the filling or the stability of the depot for acetylcholine still remains to be discovered.

A more complicated problem is presented by the action of tetanus toxin when administered by injection into a muscle in such manner and dosage as to produce a local persistent tetanus of the muscle. As A. M. Harvey has shown, the condition seems to be accounted for by lowering of the retention-level of acetylcholine in the nerve-ending depots and a concomitant loss of cholinesterase from their neighbourhood so that acetylcholine leaks continuously on to the motor end-plates, while the arrival of a nerve impulse at the endings elicits only a weak but repetitive twitch from the muscle. When the tetanus is abolished by curarine the muscle responds normally to direct stimulation. It does not seem possible to account for such a condition by any elaboration of the electrical theory of neuromuscular transmission.

It is instructive to note the kind of explanation the chemical transmission theory offers for the previously obscure apparent antagonism between physostigmine (eserine) and a partially paralytic dose of curarine. There seems to be no reason to suppose that physostigmine directly interferes with the depression by curarine of the sensitiveness of the muscle end-plate to acetylcholine. The position seems rather to be that in partial curarization the amounts of acetylcholine making effective contact with the end-plates fall below the stimulation threshold for many of these, and for a greater proportion of them with the smaller, though normally still supraliminal, charges of acetylcholine which are released by the later stimuli of a series. When physostigmine is given and depresses the cholinesterase in the neighbourhood of the depots it allows the acetylcholine reaching the end-plates again to rise above the stimulation threshold for a larger proportion of them, and even perhaps by its persistence to cause a repetitive response of some and thus still further to raise the total tension of the resulting "twitch" towards the normal.

Anticholinesterases in Myasthenia Gravis

Probably the best example of the application of the chemical transmission theory to the elucidation of a morbid neuromuscular defect is afforded by myasthenia gravis. It was shown by Blake Pritchard that the response of a myasthenic muscle to rhythmic stimulation of its nerve was very similar to that of one which had been partially paralysed by curare. Some years later Mary Walker was led by descriptions of the alleviation of such effects of curare by physostigmine to try the latter and its synthetic analogue, known by the proprietary name "prostigmin," in the treatment of myasthenia. The evidence for the transmitter function of acetylcholine and for the part played therein by cholinesterase was at the time becoming more generally known. It was natural, therefore, to connect the demonstrated relief of the myasthenic condition by physostigmine and its analogues with the action of these substances—their only common and specific action, indeed—in depressing cholinesterase and thus protecting acetylcholine. More recently other substances, such as di*iso*propyl-fluorophosphonate (D.F.P.) and tetramethyl-pyrophosphate, having nothing in common with physostigmine and its more immediate analogues other than a powerful anticholinesterase action, have proved to be similarly effective, and we shall hear more about these later this morning.

It was natural to look for evidence of an abnormal amount of cholinesterase in the blood of the myasthenic, but a number of such attempts failed to produce evidence of significant departure from the normal average in this respect; nor have muscle biopsies given any clearer indication. We seem at present to be left with several possibilities:—(1) It is not yet quite excluded that cholinesterase may be abnormally abundant in effective relation to the acetylcholine depots, though failure to find it in excess where it can be measured has rendered this unlikely; (2) there may be a defect of synthesis of acetylcholine and in consequence a defective replenishment of the depots at the nerve endings; (3) the sensitiveness of the muscle end-plates to acetylcholine may be lowered, as in partial poisoning by curarine—it may even be thus reduced by the action of an endogenous curarizing poison.

It will be clear that the remedial effect of the anticholinesterases could be accounted for by any one of these conditions, and thus affords no help in choosing among them. Experiments by Harvey and Lilienthal on the effects on the hand and forearm muscles of injecting acetylcholine directly into the brachial artery at the elbow seemed at first to suggest that the myasthenic muscles had an abnormally high sensitiveness to acetylcholine thus applied, giving a response to it which recalled that of a muscle at an early stage of the degeneration of its motor nerve. If this suggestion had been maintained it would have pointed to a defective storage of acetylcholine at the nerve endings, and thus to the causation of the myasthenia by a defect on the nervous side of the synapse. Later study of these responses has made it doubtful whether the contrast with that of the normal muscle is really of this kind—whether in fact the normal muscle is not more sensitive and in consequence more susceptible to the secondary depressant action of acetylcholine in the large arterial doses in which it was injected. If that were so the condition would be really like a partial paralysis by curare, causing a defect on the muscle side of the synapse, and the provenance of the poison causing it would become a matter of central interest. We could not, of course, overlook the possibility of the production of such a poison by an abnormally persistent thymus, the operative removal of which has been dramatically successful in a good proportion of severe cases of myasthenia though completely ineffective in others. We may hear something on the subject from Dr. Wilson, who has, I know, been examining thymuses removed by operation from myasthenics for the presence of a curarizing poison. Clearly, much more has to be discovered before we can regard the nature of this myasthenic defect as settled, but I do not think I go too far in claiming that the chemical transmission theory has helped to provide a new basis for its investigation.

Another condition, with which Dr. Brown is going to deal, is that of congenital myotonia (Thomsen's disease). I think

that the evidence which Dr. Brown will produce will show that the fault in this disease is not so much in the nature of the neuromuscular transmission as in the anomalous response of the muscle fibres to any kind of stimulus; but I do not think it can be doubted that the chemical transmission theory, and the experimental criteria based upon it, assisted a rapid analysis and clear decision in this case also.

Mention should be made also, perhaps, of the recurrent familial paralysis following a large ingestion of carbohydrate, first found by Aitken, Allot, Castleden, and Walker to be associated with a fall in the potassium content of the serum to about one-half its normal value or less and to be promptly relieved by giving potassium chloride. There was no evidence for failure of the excitatory process before it reaches the muscle, which during the paralytic crisis fails to respond to direct electrical stimulation.

Conclusion

I do not know whether anybody is going to deal in discussion with the recently advocated use of the quaternary tetra*ethyl*ammonium salts in circulatory hypertension. Many years ago Dr. Burn and I pointed out that, whereas the tetra*methyl* compounds had a powerful nicotine action, their tetra*ethyl* homologues had only a rather weak action of the curare type. Acheson recently confirmed this, emphasizing the fact that, in contrast to curarine, the tetraethylammonium salts depress the responses of the ganglion cells to preganglionic impulses and to acetylcholine more potently than they affect those of the muscle end-plates. If there is reason, then, to attribute a hyperpiesis to excessive outflow of preganglionic sympathetic impulses, tetramethylammonium salts might be expected preferentially to weaken their transmission through the ganglia.

Finally, the question which naturally excites a most urgent interest in the mind of anybody working in this field is that of the extent to which the evidence we have for a chemical transmission at the peripheral synapses provides an analogy for the mode of transmission at synapses in the central nervous system. If we are entitled to assume that cholinergic function at the synaptic endings will be marked by the presence of acetylcholine, and of the power to synthesize it, along the whole course of the fibres concerned, we can apparently conclude that the sensory fibres in the dorsal roots and tracts as far as the first synaptic connexions are definitely not cholinergic. Dr. Feldberg and Miss Vogt, on the other hand, have been finding by the same criterion evidence for a probable cholinergic function of the secondary neurones; Professor Miller is going to produce evidence of a more direct and functional kind for cholinergic transmission in the synapses of the hypoglossal nucleus and its connexions; and Professor Samson Wright is to deal with the action on central nervous functions of cholinesterases of various types. In the background, as it were, we have Professor Harvey's account of the very remarkable psychopathic effects, of the type of an anxiety neurosis, produced in man by continued treatment with D.F.P. in addition to the expected symptoms of excessive parasympathetic effects at the periphery. There is obviously a big field of possibilities here to be explored, and a need for great care and scientific discipline to prevent imaginative speculation from running ahead of the evidence. And we must not forget that, if we accept analogy as indicating, even as a working hypothesis, the probability of a chemical mode of transmission at *all* central synapses, then we must be prepared to look for transmitters other than those already recognized at the periphery and to be on the alert for their discovery.

FLOCCULATION TESTS: CHEMICAL AND CLINICAL SIGNIFICANCE*

BY

N. F. MACLAGAN, D.Sc., M.D., M.R.C.P., F.R.I.C.

Professor of Chemical Pathology in the University of London at Westminster Hospital Medical School

The application of the electrophoretic technique to pathological sera has led to the recognition of a relative increase in the serum gamma-globulin content as a fairly frequent event in certain diseases. These can be roughly divided into liver diseases—hepatitis, cirrhosis, chronic passive congestion—on the one hand, and infections on the other (Longsworth, Shedolvsky, and MacInnes, 1939; Kekwick, 1940; Gray and Barron, 1943; Olhagen, 1947; Wuhrmann and Wunderly, 1947).

In the infective group the change is particularly prominent in bacterial endocarditis, malaria, lymphogranuloma, and certain cases of plasmocytoma, and probably reflects an increase of circulating antibody. In hepatic diseases it is thought to result from abnormal protein synthesis in the liver. In many of these conditions the demonstration of gamma-globulin excess could have considerable diagnostic and prognostic importance, as it often occurs without alteration of the total globulin level or of the albumin–globulin ratio. However, for technical reasons it is impracticable to rely on electrophoresis for routine diagnostic purposes and we may profitably inquire whether any technical short cut to the required information is available.

The short cuts proposed are of course the so-called flocculation tests, and the large number of these that have been invented is perhaps an indication of the need for a reliable method of demonstrating the change in question. There are now at least nine tests that need to be considered. Listed in chronological order they are:

Formol Gel (Gaté and Papacostas, 1920)
Takata–Ara Reaction (Takata and Ara, 1926; Jezler, 1930)
Weltmann Coagulation Band (Weltmann, 1930)
Cephalin Cholesterol (Hanger, 1939)
Colloidal Gold (Gray, 1940; Maclagan, 1944a, 1946)
Thymol Turbidity (Maclagan, 1944b)
Thymol Flocculation (Neefe, 1946a; Maclagan, 1947)
Cadmium Sulphate (Wunderly and Wuhrmann, 1945)
Sharlach Red (Maizels, 1946)
Zinc Sulphate (Kunkel, 1947)

Most of these tests were invented on purely empirical grounds some years before their mechanism was understood, and it is only comparatively recently that their common chemical basis has been recognized. Although there are considerable individual variations in the different tests, it is now clear from the work of Gray (1940), Kabat, Hanger, Moore, and Landow (1943), Olhagen (1947), Maclagan and Bunn (1947), and Wuhrmann and Wunderly (1947) that they all become positive in the presence of a sufficient increase in the gamma-globulin fraction, particularly if the albumin is also reduced. The tests are technically simple and rapid in execution, and are capable of yielding results of diagnostic value within a few minutes or hours. In each case the reagent has no pronounced effect on normal serum but produces an easily observable result such as turbidity, flocculation, precipitation, or gel formation with abnormal sera.

*Based on a paper read to the Section of Physiology, including Biochemistry, at the Annual Meeting of the British Medical Association, Cambridge, 1948.

Chemical Basis of Tests

The chemical factors underlying the various tests are summarized in Tables I and II. Taking first the nature of

TABLE I

Test	Precipitating Agent	*p*H	Ionic Strength	Serum Dilution Factor
Takata–Ara	$HgCl_2$	c. 10	0·15	2–16
Formol gel	H.CHO	c. 8	0·15	1
Cephalin cholesterol	C.C. emulsion	c. 8	0·12	26
$CdSO_4$	$CdSO_4$	c. 8	0·10	1
Sharlach red	Sharlach red	c. 8	0·075	2–8
Weltmann	$CaCl_2$	c. 8	0·02–0·002	51
Colloidal gold	Colloidal gold	7·8	0·01	61
Thymol	Thymol	7·8	0·01	61
$ZnSO_4$	$ZnSO_4$	7·5	0·002	61

TABLE II

Test	Protein Fractions Active		Correlation with Total Globulin	Diseases in which Most Useful
	Precipitating	Inhibiting		
Thymol	γ-globulin	Albumin	Slight	Hepatitis
Gold	γ ,,	Albumin	,,	Hepatitis
		α and β globulin		infections
Cephalin cholesterol	(αβ)γ ,,	Albumin	,,	Hepatitis
Takata–Ara	(αβ)γ ,,	,,	,,	Liver disease
Formol gel	(αβ)γ ,,	,,	Close	Kala-azar infections
Weltmann short	αβ ,,	,,	?	Lung infections
,, long	γ ,,			Lung infections
$CdSO_4$	(αβ)γ ,,	,,	?	Infective hepatitis

the precipitating agents, these consist of salts of divalent metals ($CaCl_2$, $CdSO_4$, $HgCl_2$, $ZnSO_4$), organic protein precipitants (formaldehyde and thymol), or negatively charged colloidal solutions (gold, cephalin cholesterol, sharlach red). In the first two groups it is noteworthy that very low concentrations of reagent are employed, much lower than those ordinarily used for protein precipitation. In the case of the colloids the negative charge on the colloidal particles is unexpected in view of the similar negative charge on the protein under the conditions of the test. Evidently the reaction here is not merely one of mutual charge neutralization but must depend upon chemical differences in protein structure. As regards ease of preparation, the gold and cephalin–cholesterol reagents have given rise to certain difficulties and occasional discrepancies between the results obtained in different laboratories, but all the other reagents are easy to reproduce. A simplified method for preparation of the gold sol has recently been published (Maclagan, 1946).

The *p*H and ionic strength of the medium are all-important in these tests, and it will be seen that they all proceed in weakly alkaline solution—*p*H 7.5 to 10—and at low ionic strength (0.15–0.002). The striking effect of altering these two variables is particularly evident in the gold and thymol tests, which both work best at *p*H 7.8 and ionic strength 0.01 (Maclagan, 1944a, 1944b). These tests become quite unselective if carried out at, for example, *p*H 6 or at higher ionic strength, so that it is evidently desirable to exert an accurate control of *p*H with buffer solutions. This has been done in the gold and thymol tests but not in any of the others. Incidentally it is doubtful whether any buffer of much lower ionic strength than 0.01 would be efficient, and this level appears to be about the lowest compatible with accurate *p*H regulation. Thus the buffer proposed by Kunkel (1947), with an ionic strength about 0.001, is probably too weak to exert a decisive influence on the *p*H of the reaction mixture.

The serum dilution factor is important and is intimately connected with the last two variables. It has varied from 1 to 60 in the various tests, but the more successful ones employ a high dilution factor. Considerable dilution is in any case necessary if the test is to proceed in a buffered solution at low ionic strength, so as to avoid interference from serum electrolytes. Thus the ionic strength of serum is about 0.15 and its bicarbonate content of 0.03 M buffers it to approximately *p*H 8 when exposed to the atmosphere; a sixtyfold dilution therefore permits reasonably accurate buffering at any desired *p*H at ionic strength 0.01 if a monovalent buffer such as barbitone is used.

Electrophoretic Data

I have already mentioned the common factors of gamma-globulin and albumin which are concerned with all the tests. Table II summarizes the facts so far collected about the protein fractions active in the various tests by the workers already mentioned, and it will be seen that there are certain individual differences. Thus certain alpha and beta fractions are concerned with the cephalin–cholesterol, Takata–Ara, and formol-gel tests, while these alpha and beta fractions definitely inhibit the gold test. The thymol test appears to be simplest, since it depends only upon the albumin and gamma fractions. The Weltmann $CaCl_2$ test is really two separate tests, for according to Olhagen (1947) the shortened band indicates alpha- or beta-globulin excess while the lengthened band indicates gamma-globulin excess. Only the latter is therefore analogous to the other tests considered.

Although the data are scanty at present there are evident indications that qualitative changes in the electrophoretic fractions are important. Thus Maclagan and Bunn (1947) found that only the gamma-globulin separated from hepatitis serum produced flocculation with the thymol reagent; normal gamma-globulin gave a turbidity but no flocculation. Similarly in this work it was shown that only the hepatitis (alpha plus beta) fractions precipitated the cephalin-cholesterol and Takata reagents; normal alpha and beta fractions did not. There were also differences in the albumin fractions, normal albumin inhibiting the thymol turbidity test while hepatitis albumin did not. Similar differences in the inhibitory power of albumin fractions from different patients were noted by Guttman *et al.* (1947) and Moore *et al.* (1945) in a study of the cephalin–cholesterol test.

In apparent contradiction to the work on the thymol test discussed above are the results of Cohen and Thompson (1947) and Kunkel and Hoagland (1947), showing a fall mainly in the beta-globulin content of sera treated with the thymol reagent. However, since it is generally agreed that isolated beta fractions do not react with thymol, the significance of this observation is open to doubt. It may well be that the thymol removes phospholipid from the beta fraction and so produces an apparent fall in the beta-globulin. It is in fact well known that the presence of phospholipids is essential to the thymol reaction and that they are associated mainly with the beta-globulin fraction. Nevertheless, while isolated gamma-globulin plus phospholipid (or plus beta-globulin) will give a turbidity with thymol, isolated beta-globulin either alone or with added phospholipid has not done so in any experiment so far reported. It would appear therefore that the gamma-globulin is the important fraction and that the beta fraction acts only by contributing phospholipid.

As a corollary to this, occasional sera with grossly excessive lipid content may give "false" positive reactions with thymol. These can be detected by raising the ionic strength of the thymol buffer (Kunkel and Hoagland, 1947). The addition of 5% w/v of NaCl is convenient. This will abolish reactions due to gamma-globulin and will not affect those due to lipaemia.

Correlation with Total Serum Globulin

The last two columns of Table II summarize certain features which are further illustrated in Figs. 1–6. Since the tests aim at demonstrating excess of a particular type

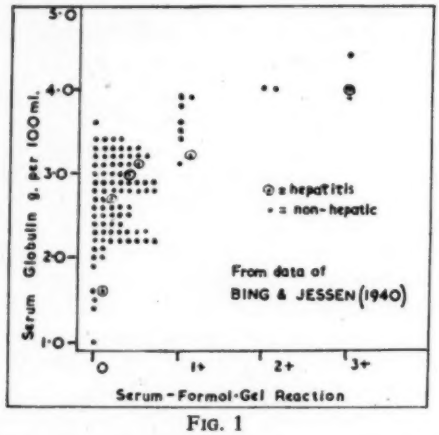

FIG. 1

of globulin it is obviously important to compare them with the total globulin estimation. The figures also illustrate the relation of the various tests to liver diseases, the hepatitis cases being shown as dots in circles and the other diseases as dots.

Taking first the formol-gel test (Fig. 1), it will be seen that all positive cases have total globulin values over

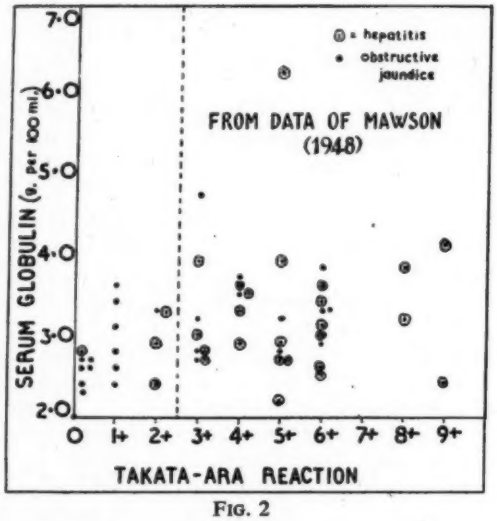

FIG. 2

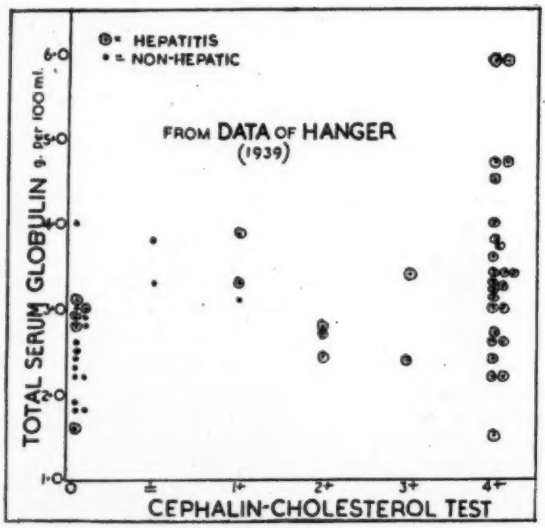

FIG. 3

3.1 g. per 100 ml., and there is no particular relation to hepatitis. This test therefore has little advantage over the total globulin estimation except that of technical simplicity. It would appear from Kunkel's (1947) report that similar remarks apply to the new $ZnSO_4$ test, although observations on this test in non-hepatic conditions are not yet available. The other tests on which similar data are available (Figs. 2–6), however, show the exact opposite—namely, a predominance of positive results in hepatitis and little correlation with total globulin. Mawson's (1948) figures for

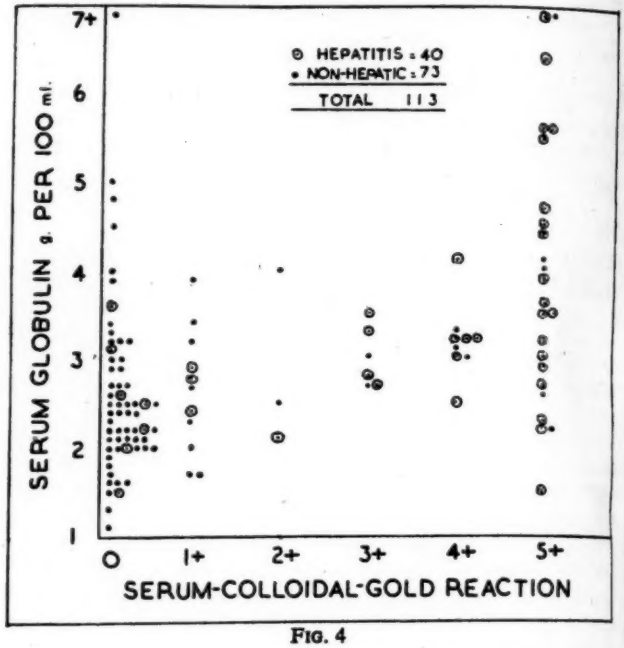

FIG. 4

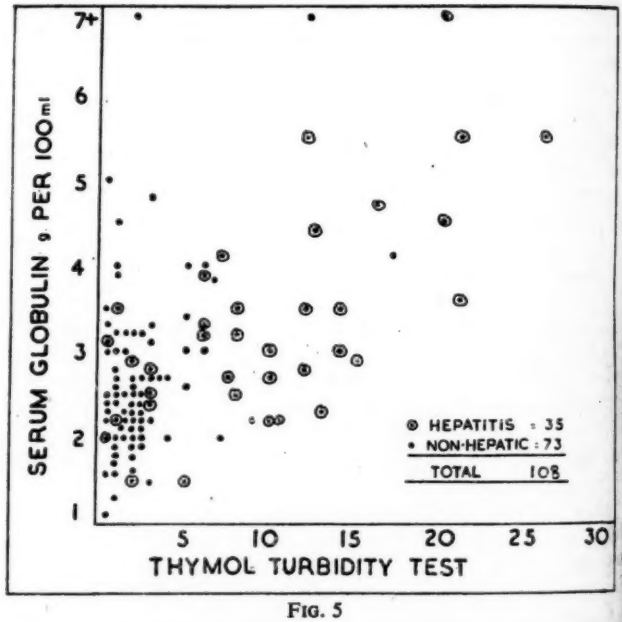

FIG. 5

the Takata-Ara reaction (Fig. 2) are not quite comparable with the others, as they refer only to jaundiced patients. It is, however, evident that with this test positive results are frequent in obstructive jaundice—i.e., in the absence of hepatitis.

Value as Liver Function Tests

The relative merits of the various tests can now be discussed, taking first their value as liver function tests. It is evident from Figs. 1–6 that the thymol, gold, and cephalin-cholesterol tests are valuable indicators of hepatitis,

as most of the positive results were recorded in this condition. Some typical reports are summarized in Table III, from which it will be seen that the sensitivity

TABLE III.—*Incidence of Positive Results in Liver Disease (% Positive)*

Disease	Thymol	Gold	Cephalin Cholesterol	Takata-Ara
Infective hepatitis	91[5], 99[8]	92[5]	66[4], 94[7], 100[2]	84[6]
Post-arsphenamine jaundice	47[5]	47[5]		
Hepatic cirrhosis	87[5]	87[5], 100[1]	71[4], 100[7]	93[3]
Obstructive jaundice ..	8[5]	8[5]	16[2], 17[4], 78[7]	41[6]

[1] Gray (1940). [2] Hanger (1939). [3] Jezler (1930). [4] Kirschner and Glickmann (1943). [5] Maclagan (1944b). [6] Mawson (1948). [7] Pohle and Stewart (1941). [8] Shank and Hoagland (1946).

of these tests in infective hepatitis and hepatic cirrhosis is very high, being in the neighbourhood of 90–100% in most of the series quoted. The proportion of positive results in post-arsphenamine jaundice is, however, much lower, being only 47% in the case of the gold and thymol tests (Maclagan, 1944b, 1944c). It seems that a similar preponderance of negative results is found in homologous serum jaundice (Neefe, 1946b), and this difference fits in

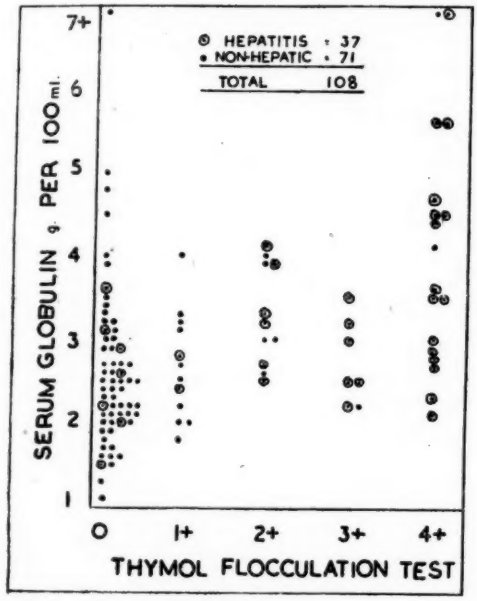

FIG. 6

well with the very definite immunological difference that has been demonstrated between infective hepatitis and homologous serum jaundice, which are now thought to be due to different viruses (Neefe, Stokes, and Gellis, 1945). The Takata–Ara reaction gives somewhat similar results to the others in cirrhosis, but has not been so widely used in acute hepatitis.

The results in obstructive jaundice are, however, very different with these four tests, thymol and gold giving mainly negative results, while cephalin cholesterol and Takata–Ara are often positive (16% to 78%). This gives a definite advantage to the thymol and gold tests for the special purpose of investigating jaundice of doubtful origin, a field in which they have proved very useful (Maclagan, 1947).

The detection of residual hepatitis after an acute attack is another example of where the thymol test has found particular application, as shown particularly in the work of Neefe (1946a), who found that the thymol flocculation test may remain positive for as long as a year after an attack of acute hepatitis, being associated in this case with residual symptoms and biopsy evidence of hepatitic damage.

The other tests mentioned seem to be less useful in the diagnosis of liver disease, although reports are in some cases conflicting or incomplete. It is claimed that the Sharlach-red test gives results very similar to the gold test (Maizels, 1946 ; Ducci, 1947), and the $CdSO_4$ test has found some application in hepatitis (Wuhrmann and Wunderly, 1947). The large literature on the Takata–Ara reaction was reviewed by Magath (1940). The $CaCl_2$ test has found most application in non-hepatic conditions.

Value in Non-hepatic Conditions

All the tests tend to give positive results in infections of the type mentioned above, and such results may often be of diagnostic value. Thus the formol-gel test has been found useful in kala-azar (Napier, 1921), and the Takata–Ara reaction was originally used in pneumonia, in which it was said to help in differentiating lobar pneumonia from bronchopneumonia (Takata, 1925). The Weltmann test is said to indicate "exudative" or "fibrotic" changes, and has been particularly employed in lung infections in a manner rather similar to the sedimentation rate (Gradwohl, 1943). The $CdSO_4$ test has also been applied in this field.

Results of this type are perhaps less frequent with the gold, thymol, and cephalin–cholesterol tests, but they are by no means absent, and the gold test in particular has given a high percentage of positive results in heart failure, malaria, infective endocarditis, glandular fever, and rheumatoid arthritis (Carter and Maclagan, 1946). The cephalin–cholesterol test is also usually positive in malaria (Fredricks and Hoffbauer, 1945) and the thymol test in glandular fever (Cohn and Lidman, 1946). Such results can be of diagnostic help—for example, in a case of febrile rheumatic carditis with infective endocarditis as a possible complication positive flocculation tests would favour the graver diagnosis. In the infective group as a whole the tests probably depend mainly on antibody production and give easy and rapid evidence of this process. In heart failure, glandular fever, and possibly malaria, on the other hand, they probably reflect a true hepatic involvement in the disease and may have some prognostic value, particularly in heart failure. The unexplained high proportion of positive gold tests in rheumatoid arthritis is entirely different from the mainly negative findings in spondylitis ankylopoietica, and forms a useful point of distinction between these two diseases (Hart *et al.*, 1948).

The possible application of the tests in protein chemistry and in immunology has been little explored. If they can detect differences between protein fractions which are electrophoretically identical they must have some contribution to make to the characterization of proteins in general. Thus they have already been able to show differences between all the electrophoretic practices obtained from normal and hepatitis sera respectively. In this sense they may form a useful addition to the electrophoretic method.

Discussion

The principal result of the work which has been reviewed here is that this group of tests can now be seen as a whole and an attempt made to assess their value. It would seem that they are now entitled to be lifted from the realm of doubtful and mysterious procedures to the status of practical short cuts to the demonstration of a particular type of protein change in the serum. This may be described as a relative gamma-globulin excess, and the finding is of great diagnostic help in hepatitis and is of theoretical interest in various infective conditions. The possible clinical value in infections needs to be explored by further study. The information obtained from the tests is additional and complementary to the usual serum protein estimations, and the

proportion of positive results in the conditions indicated is in general much higher than the incidence of high total globulin values or of changes in the albumin–globulin ratio. On account of the non-specific nature of the tests they must always be interpreted with due regard to the general clinical background, a proviso which would of course apply to most laboratory investigations.

As regards the relative merits of the various tests there is room for considerable difference of opinion. However, from the physico-chemical angle it can be said that the conditions are more accurately controlled in the case of the thymol and colloidal-gold tests, in which the *p*H and ionic strength are kept at optimum levels by means of buffer solutions. Study of purely clinical data suggests that the gold, thymol, and cephalin–cholesterol tests all have certain advantages, but in the study of liver disease the thymol test appears at present to be slightly superior. It also has the advantage that the reagent is easier to prepare than either of the other two. Most of the other tests mentioned are probably not so reliable as "liver function tests" but have found useful applications in the study of certain infections. The position of the sharlach-red and zinc-sulphate turbidity tests needs to be elucidated by further study.

There is a certain advantage for routine purposes in using two tests of slightly different character, and my present preference is for the thymol (turbidity and flocculation) and the gold tests. The former is fairly specific for liver disease, the latter gives a greater sensitivity in conditions such as rheumatoid arthritis. However, the gold test might well be replaced by the cephalin–cholesterol test or possibly one of the other tests if difficulty is experienced in making up the gold sol. All the tests are so similar in principle that it is to be hoped that some degree of standardization will be eventually achieved; the ideal would be a single accepted test for demonstrating gamma-globulin excess.

Summary

The chemical mechanism underlying the various flocculation tests has been considered, and the essential similarity of these tests is emphasized.

All the tests are influenced positively by serum gamma-globulin and negatively by albumin. The alpha- and beta-globulin fractions do not influence the thymol test but have a variable effect on the others.

The formol-gel and $ZnSO_4$ tests are closely correlated with total serum globulin, the others have little correlation with total globulin.

The relative value of the various tests as indicators of hepatic dysfunction and of antibody formation is discussed.

REFERENCES

Bing, J., and Jessen, C. U. (1940). *Acta med. scand.*, **105**, 273.
Carter, A. B., and Maclagan, N. F. (1946). *British Medical Journal*, **2**, 80.
Cohen, P. C., and Thompson, F. (1947). *J. Lab. clin. Med.*, **32**, 314.
Cohn, C., and Lidman, B. I. (1946). *J. clin. Invest.*, **25**, 145.
Ducci, H. (1947). *J. Lab. clin. Med.*, **32**, 1273.
Fredricks, M. G., and Hoffbauer, F. W. (1945). *J. Amer. med. Ass.*, **128**, 495.
Gaté and Papacostas (1920). *C.R. Soc. Biol., Paris*, **83**, 1432.
Gradwohl, R. B. H. (1943). *Clinical Laboratory Methods and Diagnosis*, 3rd ed., Kimpton, London.
Gray, S. J. (1940). *Arch. intern. Med.*, **65**, 524.
—— and Barron, E. S. G. (1943). *J. clin. Invest.*, **22**, 191.
Guttman, S. A., Potter, H. R., Hanger, F. M., Moore, D. B., Pierson, P. S., and Moore, D. H. (1945). Ibid., **24**, 296.
Hanger, F. M. (1939). Ibid., **18**, 261.
Hart, F. D., Robinson, K. S., Allchin, F. M., and Maclagan, N. F. (1948). In preparation.
Jezler, A. (1930). *Z. klin. Med.*, **114**, 739.
Kabat, E. A., Hanger, F. M., Moore, D. H., and Landow, H. (1943). *J. clin. Invest.*, **22**, 563.
Kekwick, R. A. (1940). *Biochem. J.*, **34**, 1248.
Kirschner, P. A., and Glickman, S. I. (1943). *J. Lab. clin. Med.*, **28**, 1721.
Kunkel, H. G. (1947). *Proc. Soc. exp. Biol., N.Y.*, **66**, 217.
—— and Hoagland, C. L. (1947). *J. clin. Invest.*, **26**, 1060.
Longsworth, L. G., Shedolvsky, T., and MacInnes, D. A. (1939). *J. exp. Med.*, **70**, 399.
Maclagan, N. F. (1944a). *Brit. J. exp. Path.*, **25**, 15.
—— (1944b). Ibid., **25**, 234.
—— (1944c). *Proc. R. Soc. Med.*, **37**, 460.
—— (1946). *Brit. J. exp. Path.*, **27**, 369.
—— (1947). *British Medical Journal*, **2**, 197.
—— and Bunn, D. (1947). *Biochem. J.*, **41**, 580.
Magath, T. B. (1940). *J. Lab. clin. Med.*, **26**, 156.
Maizels, M. (1946). *Lancet*, **2**, 451.
Mawson, C. A. (1948). *J. clin. Path.*, **1**, 167.
Moore, D. B., Pierson, P. S., Hanger, F. M., and Moore, D. H. (1945). *J. clin. Invest.*, **24**, 292.
Napier, L. E. (1921). *Indian J. med. Res.*, **9**, 830.
Neefe, J. R. (1946a). *Gastroenterology*, **7**, 1.
—— (1946b). *Med. clin. N. Amer.*, **30**, 1407.
—— Stokes, J., jun., and Gellis, S. S. (1945). *Amer. J. med. Sci.*, **210**, 561.
Olhagen, B. (1947). *Acta med. scand.*, Suppl., **196**, 478.
Pohle, F. J., and Stewart, J. K. (1941). *J. clin. Invest.*, **20**, 241.
Shank, R. E., and Hoagland, C. L. (1946). *J. biol. Chem.*, **162**, 133.
Takata, M. (1925). Transactions of 6th Biennial Congress Far Eastern Ass. Trop. Med., Tokyo, Vol. 1, p. 693.
—— and Ara, K. (1926). Cited by Jezler (1930).
Weltmann, O. (1930). *Med. Klin.*, **26**, 240.
Wuhrmann, F., and Wunderly, C. H. (1947). *Die Bluteiweisskörper des Menschen*. Schwabe, Basle.
Wunderly, C., and Wuhrmann, F. (1945). *Schweiz. med. Wschr.*, **75**, 1128.

THE CONSERVATIVE TREATMENT OF PLACENTA PRAEVIA

BY

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In every discussion on the treatment of placenta praevia there are two fundamental questions to be answered—namely, what to do and when to do it. The former has fortunately been simplified with the increasing safety of the lower-segment caesarean operation, and the procedure of choice will usually be either rupture of membranes or abdominal delivery. However, the optimum timing of this intervention remains a matter of opinion on which authorities are at variance. It has long been taught, with considerable emphasis in many schools, that expectant treatment of a diagnosed or suspected placenta praevia can never be countenanced. This principle has been based upon the not unnatural supposition that a patient with a major degree of placenta praevia would in the absence of intervention frequently bleed to death, and that fatal haemorrhage might ensue at any time without warning. Evidence is accumulating, however, to suggest that more tragedies are produced nowadays by overtreatment than by neglect, and that in some cases delay might even benefit mother as well as foetus; for in the borderline case rupture of forewaters can be performed with far more confidence when it has been possible to delay until the uterus is contracting and the cervix open.

An American obstetrician (Johnson, 1946), in an enthusiastic overstatement to prove his case, has promised a reward for records of any case of placenta praevia in which death from haemorrhage has followed strict non-intervention in all stages of labour. It has apparently not been claimed, but this does not necessarily prove anything, since no doctor could remain idle in expectation of seeing his patient die from haemorrhage. This helps to emphasize the fact that there are natural ways of arrest of haemorrhage from a placenta praevia. In rare instances the placenta may actually be delivered spontaneously in front of the foetus with remarkably slight blood loss (Lloyd, 1947, reported below). It cannot be denied that some cases of placenta praevia have sudden haemorrhages which may be most alarming and require urgent blood transfusion if the uterus is not emptied as a routine as soon as the condition is suspected. On the other hand, a period of delay might facilitate treatment and decrease the number of caesarean sections, and it assuredly *will* lower the appalling foetal loss from prematurity.

A brief review will be given of the recent pertinent literature and a series of 100 cases presented in an effort to assess the advantages and risks to mother and child that may be expected with conservative treatment.

Recent Literature

Probably the finest series of cases in which treatment was based strictly on the old principle of immediate intervention was reported from Chicago by Davis and Campbell (1946). Treatment was generally confined to caesarean section or rupture of the membranes according to the position of the placenta as felt on vaginal examination shortly after the patient had been admitted to hospital; maternal mortality was as low as 0.6% (two deaths in 325 cases), which compares extremely favourably with the figure of 5.9% compiled by Professor F. J. Browne (1946) from 3,103 cases in recent records of 11 British teaching hospitals. The caesarean section rate was 40%, and blood transfusion was given to 40% of patients (a high figure). Quoting a foetal mortality of 32%, the authors state that "the most important cause of foetal death was prematurity," and "the premature infant has been considered expendable to ensure the greatest possible safety for the mother." Although this figure for foetal loss is decidedly better than that of 54.2% in Browne's series, it is not nearly low enough; and other authorities claim that judicious conservatism will give equally good maternal results with considerably improved chances for the baby.

Expectant treatment was championed simultaneously on both sides of the Atlantic by Macafee (1945) and Johnson (1945). Both based their treatment on the contention that *in the absence of vaginal manipulation* the first haemorrhage from a placenta praevia will never be fatal, and subsequent haemorrhages will not be fatal so long as the haemoglobin level of the blood is normal at the onset of bleeding. Macafee reported a personal series of 174 cases with one death and a foetal loss of only 23.5%; yet this figure included six foetal abnormalities and nine other cases in which the low implantation of umbilical cord into placenta made foetal death almost inevitable after a severe haemorrhage: an improved figure for foetal loss of only 6% was achieved in the last 47 cases. This revolutionary conception of foetal risk was attained by extreme conservatism: the principle was laid down that no vaginal examination should be made unless and until it could be followed immediately by whatever treatment was required for delivery (e.g., caesarean section). Thus a patient would be put to bed to wait until the last few weeks of pregnancy, regardless of repeated "warning" haemorrhages so long as there was no undue anaemia; and with increasing experience there was less cause for alarm over any one apparently severe attack of bleeding. Macafee states significantly that "among these patients there has been nothing to confirm the belief that recurrent haemorrhages tend to lead up to one catastrophic haemorrhage." He permitted a period of delay in over half the cases, one patient spending 14 weeks in hospital, while another had nine attacks of bleeding; yet blood transfusion was required in only 13% of patients, and 39% (not a high figure) were delivered by caesarean section.

Johnson (1945) treated 79 cases of placenta praevia without a maternal death and with loss of 22% of babies. His relatively high (53%) caesarean section rate is an index of his reluctance to interfere vaginally in any way at all, and his dictum, "a non-traumatized placenta praevia will not cause fatal haemorrhage," sums up his general attitude.

In an attempt to check the validity of Macafee and Johnson's contentions, Yepes and Eastman (1946) summarized 304 cases that had been treated during the past half-century along conventional lines in the Johns Hopkins Hospital. The maternal mortality had been reduced during the period from 13.8% to 0.9%, but the foetal loss had improved only from 78.5% to 46.8%. They found that in no instance had an initial or subsequent haemorrhage been the cause of death except in association with extensive vaginal manipulation; and that the only patient to die undelivered (in 1920) had refused treatment, had become profoundly anaemic from four subsequent attacks of haemorrhage at home, and had finally died after vaginal manipulations.

Daichman and Pomerance (1947) reported a series of 165 cases over an eleven-year period, with one maternal death and a foetal loss of 26%. They attribute their good results to a rather liberal use of caesarean section (59%) and a gradual increase in expectant treatment. They consider that it is safe to temporize "when the infant is near viability," implying that repeated haemorrhage is less likely to occur before the last few weeks of gestation: this may not be altogether true, but it serves to underline their approval of at least a limited conservatism.

Finally, Williams (1948) reported a series of 105 cases with only one maternal death over an eleven-year period; the foetal loss was 28% and the caesarean section rate 42%. However, there were 41 cases (39%) treated expectantly, and of these the foetal mortality was only 12%. He thus endorses the great improvement in foetal chances of survival that may be expected with this treatment.

After such apparent success of varying degrees of conservative treatment it was disappointing to hear reactionary views from Scotland expressed by Sturrock, Stirling, and Tennent (1947). A series of 228 cases was quoted from Edinburgh with only two maternal deaths but a foetal loss of 39%; conservative treatment had been practised in 6%, and the authors express no enthusiasm for it on account of "the close vigilance required and the smooth and speedy application of appropriate treatment essential in the presence of the sudden further haemorrhage." The Glasgow school, quoting 505 cases, in 27% of which there had been at least 24 hours' delay before instituting active treatment, was very discouraging: the overall figures showed 18 maternal deaths, 34% foetal loss, and 55% caesarean sections, while in the delayed group there was a slightly higher foetal loss with considerably greater maternal morbidity. The significance of these results may perhaps be offset by the selection of their group for delayed treatment, so that direct comparison of results between the two groups is not applicable. Another factor that might have affected the expectant group adversely is a variation from the more usual management of this type of case: vaginal examination of the more serious cases was conducted under anaesthesia in only 1 or 2% of patients.

To conclude this summary of available evidence it may be stated that most of the obstetricians who have reported their experiences of the expectant treatment of placenta praevia appear to have been favourably impressed with the results.

Personal Experience

In the following report a small series of cases has been analysed in an attempt to ascertain how nearly the results of Macafee and Johnson can be equalled in a busy hospital in which responsibility for emergencies devolves upon all members of the honorary staff. It is obvious that the principles of conservative delay (with its worries and disadvantages) are unlikely to be accepted as quickly and comprehensively as when all experience is gained and all responsibility accepted by one man. It is therefore encouraging to record a consecutive series of 100 cases of placenta praevia (95 in 1947 and 5 in 1948) treated at

the Birmingham Maternity Hospital by six members of the staff with no maternal deaths and the loss of only 17 out of 103 babies (stillbirths and neonatal deaths in hospital). There had been no maternal death from placenta praevia in the three years prior to this series.

The principles of treatment were as follows. There was general agreement among the staff that so far as possible no infant should be delivered before about the 37th week of gestation, although, if the foetus appeared to be very well developed and there were other indications, a week or two earlier might be allowed. After the 37th week it was considered that the risks to the foetus of asphyxia following a severe haemorrhage, and the now unnecessary loss of blood to the mother, outweighed the advantages of the last few possible weeks *in utero*; consequently a severe haemorrhage in the last three or four weeks was considered an indication to empty the uterus: before this it called for conservative treatment. However, there was considerable divergence of opinion among the staff about the wisdom of continued delay in the face of repeated haemorrhage, and inevitably there were occasions on which active intervention was deemed advisable in maternal interests when another surgeon might have advised procrastination still further.

The usual procedure in the case of haemorrhage before the 37th week was to admit the patient to hospital, examine the cervix with a speculum, give morphine as required, and wait for bleeding to stop; the haemoglobin level was checked, the blood grouped and the rhesus test performed, and blood cross-matched for transfusion in the more serious cases. After several days without further loss primigravid patients were often sent home to bed, and most cases with only a slight loss before the 32nd week were allowed up and sent out with instructions that in the event of further haemorrhage they should go straight to bed and discourage any vaginal examination. No attempt was made at radiographic diagnosis of the placental site. No vaginal examination was to be made in hospital until the formal procedure under an anaesthetic with the theatre set for caesarean section, generally after the 36th week. The date of this examination depended on the size of the baby, the recurrence of haemorrhage, and the attitude of the surgeon to repeated blood loss; and also on the reaction of the foetal heart to each attack of haemorrhage. As a general rule the procedure adopted was caesarean section for cases in which the placenta was palpated across the cervix or coming up to its margin (the second, third, and fourth degrees of Professor F. J. Browne), with rupture of membranes for the others. Sometimes a second-degree case in a multipara would be treated by rupture of membranes with application of Willett's forceps to the scalp, or bringing down a leg of a flexed breech if this could be done easily through a dilating cervix; thus one would be able to exert traction on the presenting part should the bleeding be uncontrolled. Bipolar version and subsequent breech extraction was employed only twice, on patients whose babies were already dead.

The anaesthetic for the examination was generally thiopentone, and it was usually followed by gas–oxygen–ether or "trilene" for the section; a number of severe cases in which the diagnosis appeared self-evident, however, were operated on under spinal or local analgesia without any vaginal examination in an effort to avoid further foetal distress. The lower-segment operation was generally used. Blood transfusion was given freely, being set up before the vaginal examination in all cases of dangerous haemorrhage: it was used in 21 cases, including three occasions for post-partum haemorrhage following vaginal delivery. Statistics are given in Table I.

Conservative Treatment

Macafee quotes a figure of over 50% for cases of placenta praevia in which conservative treatment was practicable. This was by no means so in the series under consideration. There were two reasons: in the first place, the majority of patients had already experienced one or more attacks of bleeding before admission, and successful (though often ill-advised and hazardous) conservative treatment had been practised by their practitioners; consequently the majority of those admitted were already in the last month of pregnancy. Secondly, a distressingly large number of patients had already been examined vaginally outside hospital, and this misplaced active intervention had often produced serious exacerbation of haemorrhage and sometimes foetal distress. There were in fact only 26 patients (27 babies) admitted with bleeding before the 36th week, and as one patient was already in labour and two babies were dead there were only 24 cases in which it is considered that planned conservative treatment was possible. These are summarized in Table II.

TABLE I.—*Statistical Summary*

Cases of placenta praevia	100
Babies delivered	103
Maternal deaths	0
Foetal and neonatal loss	17 (16·5%)
Types of placenta:	
1st degree	43
2nd "	28
3rd "	25
4th "	4
Primigravidae	32
" with 1st degree placenta praevia	19 (59%)
Treatment:	
Caesarean section (including 2 following A.R.M.)	47
A.R.M. alone	22
A.R.M., Willett's forceps*	5
A.R.M., bringing down leg*	5
Internal version and extraction	2
Non-intervention†	14
Forceps delivery†	4
Craniotomy†	1

* Subsequent traction rarely required.
† No treatment needed for haemorrhage.

TABLE II.—*Conservative Treatment*

Conservatism possible	24	
" not used	4	(foetal loss 3)
" attempted	20	(" " 3)
" abandoned within 7 days	4	(" " 0)
" persisted for over 7 days	16	(" " 3)

Maternal Prognosis

The maternal prognosis under the conservative regime has not apparently deteriorated in any way, and in very few cases was there ever cause for the slightest alarm; this may have been partly due to a natural reluctance to continue procrastination in the face of repeated bleeding, but the morale of the resident staff, as well as the safety of the patients, was certainly maintained by a good supply of readily available blood for transfusion. On several occasions there was a sudden loss of 15–20 oz. (425–570 ml.) of blood, usually in the middle of the night, but experience soon confirmed Macafee's statement that these haemorrhages are not catastrophic. In fact it can be categorically stated that in no instance was maternal life endangered by conservative treatment: there were no deaths and no "near deaths." In the 16 cases in which conservatism was practised for a week or more, in hospital or after discharge home, the maximum period of delay was 8 weeks and the average 17 days. Of the four cases in which active treatment was adopted in less than a week two had recurrent haemorrhage, one had pre-eclamptic toxaemia, and one had spontaneous premature labour.

Foetal Prognosis

The reduction of foetal loss is the real justification of conservative treatment, and the figure of 16.5% compares favourably with F. J. Browne's collected figure of 54% and with other series where active intervention has been adopted. That the improvement chiefly affects the premature component of the foetal death rate is shown by the 24 quoted cases in which the patient was admitted before the 36th week and conservatism was possible: when it was practised the loss was 15%, and when it was neglected the loss was 75%. The whole subject of foetal death in relation to placenta praevia is so important that an analysis has been made of the cases in this series, and an effort has been made to determine how far foetal

TABLE III.—*Analysis of the 17 Foetal Deaths*

Associated with prematurity	6
Possible mismanagement	5
Misfortune	1
Apparently inevitable	5

mortality may be reduced by conservative strategy and skilled tactics and what may be the hard core of inevitable loss. Table III gives a rough classification of the 17 cases.

In any discussion on the inevitability or otherwise of foetal death it is essential that outside practitioners and hospital staff should be considered together as one therapeutic unit. In

case should loss of a baby be classed as inevitable on the grounds that the damage was done before admission to hospital, and it is only by a consideration of the mistakes of the practitioners, as well as the possible accidents or errors committed inside hospital, that a true estimate of optimum foetal prognosis may be made.

There were six foetal deaths associated with prematurity, and four of these patients had had vaginal examinations which had precipitated further bleeding before admission; in one case the foetus was dead on admission and in another the patient was already in labour, though it is difficult to be certain how far these facts are attributable to intervention. In the other two cases which had already been examined it was decided that conservative delay was unlikely to be successful, and both were examined under anaesthesia, followed by section for one and rupture of membranes for the other. Of the two patients who had had no intervention, one was kept in hospital for two weeks (29th to 31st) and then delivered because of repeated minor haemorrhage; the other (at the 34th week) was delivered at once. Both had caesarean sections and both infants died as the result of prematurity. It is probable that if intervention had been longer delayed the chances of survival of these two infants would have been materially increased, with little, if any, added maternal risk.

It is unfortunately necessary to record five cases in which foetal death followed mismanagement in some stage of the patient's treatment either by the practitioner outside or by the resident staff in hospital. The first, a 3-gravida with no living children, had four "warning" haemorrhages in the last month of pregnancy before a final severe bleeding for which she was admitted in labour at term; there was profound foetal asphyxia, and despite immediate caesarean section the child failed to survive. At operation it was found that the cord was inserted into the placenta immediately over the internal os. This case serves to emphasize that in the last weeks of pregnancy conservative treatment may not be in the interest of the foetus. The second case illustrates the same lesson. A 2-gravida was admitted following an initial severe haemorrhage at the 38th week. There was no foetal distress, and examination was delayed on account of other supposedly more urgent work, but three hours later the foetal heart rate fell to 104 and caesarean section, though urgently performed, failed to save the child; it lived for a few hours, and necropsy showed severe asphyxial changes in the viscera. The third case (reported elsewhere, Mills, 1948) was one of vaginal delivery of a multipara despite a third-degree placenta praevia. Premature rupture of membranes without bleeding had led to the erroneous conclusion that the os must be at least partly covered by membranes, and the patient was delivered by traction on Willett's forceps, which controlled bleeding but asphyxiated the baby. Finally, there were two cases in which bad technical errors were made. A baby was lost from cerebral haemorrhage during forceps extraction at the 36th week following two weeks' successful conservative treatment of a primigravida; and a foetus died from asphyxia in the first stage of labour owing to compression of a posterior placenta praevia by the descending head in a primigravid patient in whom placenta praevia had not been suspected. These five cases represent five unnecessary foetal deaths.

The one case of "misfortune" was an 8-lb. (3.63-kg.) baby which died from neonatal infection when a fortnight old.

There were five cases in which foetal death appears to have been unavoidable. Two of these were cases of vasa praevia, in one of which only the first of twins was lost, while in the other there was no haemorrhage until the presenting vessel was torn with the rupture of the membranes early in labour. There was one hydrops foetalis. One case appeared to be an association of placenta praevia with accidental retroplacental haemorrhage and rapid foetal asphyxia. The final case (reported elsewhere, Lloyd, 1947) was one in which the placenta became fully separated early in labour with no alarming haemorrhage and was found lying loose in the vagina at examination for an impacted shoulder presentation.

There is thus reason to believe that with good luck, more skilful management, and a more resolute adoption of conservative principles the foetal loss in the cases outlined above might have been reduced from 17 to 7 without in any way increasing the maternal dangers.

Conclusions

The number of cases of placenta praevia in which it is possible and advisable to adopt conservative measures depends upon the stage in pregnancy at which the patient is sent to hospital for advice. If this is sought after the first haemorrhage, and there has been no previous intervention, Macafee's experience shows that deferring of active treatment may be practicable in over 50% of cases; but if, as is shown in this series, there has already been procrastination or examination before admission, then this number may be reduced to about 25%.

Conservative treatment has advantages and disadvantages for the mother; the latter are the more obvious. She must either be confined to hospital or lead a very restricted existence at home for a number of weeks, and she may sometimes be required to suffer further haemorrhage; on the other hand, there is little, if any, increased danger to life, and there is a slightly lower chance of the need for delivery by caesarean section. If, however, caesarean section should eventually become necessary there is a much greater probability that she will get a live baby in compensation.

The advantages to the foetus of conservative delay greatly outweigh the risks, since maturity is the prime requisite for foetal survival. However, it must not be forgotten that any serious haemorrhage may suddenly produce foetal asphyxia, and consequently delay of even a few hours is unjustifiable when the foetus has reached a satisfactory stage of development. Since conservative treatment has been adopted for placenta praevia the published reports show for the first time a foetal and neonatal loss below 30%.

Finally, it is considered that the careful adoption of conservative measures in suitable cases is practicable only in a hospital serving an area blessed with reasonably good transport facilities, a good blood-transfusion service, and an adequate standard of general nutrition among its patients; further, it will naturally require a sufficiency of antenatal beds and an experienced resident staff. In these circumstances, given co-operation from the local practitioners, there is every opportunity for the reduction of foetal mortality in placenta praevia to a figure in the region of 10% while the maternal mortality remains at its present minimal figure.

Summary

Recent literature relative to the conservative treatment of placenta praevia is reviewed.

A series of 100 cases of placenta praevia treated largely along conservative lines is reported; there were no maternal deaths, and the foetal and neonatal loss was 16.5%, which compares favourably with other recently reported figures.

The causes of foetal death in this series are analysed; the majority would appear to have been avoidable.

Conclusions are drawn regarding the present scope of conservative treatment.

My thanks are due to Professor Chassar Moir for helpful criticism and advice, to Miss P. Challons for assistance with hospital records, and to the honorary staff of the Birmingham Maternity Hospital for permission to publish their cases.

References

Browne, F. J. (1946). *Antenatal and Postnatal Care*. 6th ed. Churchill, London.
Daichman, I., and Pomerance, W. (1947). *Amer. J. Obstet. Gynec.*, **53**, 1024.
Davis, M. E., and Campbell, A. (1946). *Surg. Gynec. Obstet*, **83**, 777.
Johnson, H. W. (1945). *Amer. J. Obstet. Gynec.*, **50**, 248.
—— (1946). *Med. Rec. & Ann.*, **40**, 1297.
Lloyd, M. H. (1947). *British Medical Journal*, **2**, 822.
Macafee, C. H. G. (1945). *J. Obstet. Gynaec. Brit. Emp.*, **52**, 313.
Mills, W. G. (1948). *British Medical Journal*, **1**, 500.
Sturrock, J., Stirling, H., and Tennent, R. A. (1947). *Edinb. med. J.*, **54**, 496, 504, 510.
Williams, T. J. (1948). *Amer. J. Obstet. Gynec.*, **55**, 169.
Yepes, L. G., and Eastman, N. J. (1946). *Sth. med. J.*, **39**, 291.

THE DIAGNOSIS OF LATENT TETANY

WITH OBSERVATIONS ON THE EFFECT OF CALCIFEROL

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The object of this publication is to call attention to some pitfalls in the diagnosis of latent tetany and to show that the usual diagnostic methods are inadequate. A more detailed account of a new hyperventilation test which was mentioned in a preliminary communication (O'Donovan, 1945) is included.

The 34 patients studied were adults and adolescents, and almost all had chronic latent tetany. This may be important, as most writers on the subject deal with children and with acute or transient tetany. All the patients in this series had hypocalcaemia—i.e., less than 9 mg. per 100 ml. of serum calcium. With the method used (Clark and Collip, 1925) the normal serum calcium varied from 9.5 to 11.5 mg. per 100 ml., but it is fairly reasonable to presume that figures between 9 and 9.5 mg. are not definitely abnormal. Hypocalcaemia is here assumed to be synonymous with latent tetany, as none of the patients had renal disease or any gross abnormality of their serum protein. If the methods of diagnosis of latent tetany in hypocalcaemia are reliable they should also be reliable in other causes of latent tetany.

It will be noted from the Table that the number of observations exceeds the number of individual patients, since patients were usually seen at intervals of six to twelve months. Only one observation was recorded when a patient was studied daily for some days and there was no gross change in serum calcium or signs of latent tetany.

Tests for Latent Tetany on Hypocalcaemic Patients not Receiving Calciferol

	No. of Patients	No. of Observations	No. of Positive Reactions	Positive	Negative
Chvostek's sign ..	30	85	23	27%	73%
Trousseau's sign ..	32	89	59	66%	34%
Combined test ..	13	27	23	85%	15%
Trousseau's sign and the combined test where necessary	32	58	55	95%	5%

The patients' hypocalcaemia was due to surgical hypoparathyroidism (14 cases), apparent idiopathic hypoparathyroidism (2 cases), or calcium deficiency (18 cases). The last-named were mostly cases of idiopathic steatorrhoea, although dietary deficiency may have influenced some. When patients were given calciferol (50,000 to 100,000 units daily) the calcium intake was kept at an approximately normal level by instructing them to take half a pint of milk daily in addition to the usual diet.

Signs of Latent Tetany without Calciferol Therapy

Erb's sign of electrical excitability is not considered here, as it is not a feasible procedure in ordinary clinical examinations. It is unreliable in minor degrees of latent tetany in which an improved method of diagnosis is needed. It is also not so objective and clear-cut as some descriptions would lead us to believe.

Chvostek's sign is so unreliable that its sole merit is its convenience. In only 27% of observations (see Table) was it found positive. If it has any value it is in recent or acute tetany, as it was observed to be strongly positive in 9 out of 11 cases of hypoparathyroidism within three days after thyroidectomy. It is considered that when the tap on the facial nerve causes contraction around the mouth, nose, and eyes (+ 3 response) there is very satisfactory evidence of latent tetany and biochemical investigation is indicated. A negative or trace reaction involving the upper lip is of no significance, and should not exclude the other clinical tests for tetany.

Trousseau's Sign

This was found positive in 66% of observations (see Table). It is very dependable, as it is rarely positive in normal subjects. It is, however, sometimes positive in people of a hysterical type or in workers whose hands are held in a semi-tetanic position for some hours daily—e.g., seamstresses, cobblers, and glove or leather stitchers. Another source of error may be avoided if the test is always done on the arm that is more often used, as it is rarely positive on that side only (O'Donovan, 1945).

The technique of Trousseau's sign is seldom described adequately. The tourniquet should be applied at greater than systolic blood pressure so that the radial pulse is obliterated. This should be checked during the test. The tourniquet should be applied without painful nipping of the skin, and a sphygmomanometer is therefore advisable. For a very obese or heavy muscular arm a pressure pad may be applied on the brachial vessels and nerves. The presence of carpal spasm should be checked by feeling the muscles, as an experienced patient may voluntarily assume the position. If no cramp appears after four minutes the test may safely be considered negative.

The Hyperventilation Test

Various attempts have been made to utilize the response to hyperventilation as a diagnostic aid in latent tetany. Most authors mention the induction of tetany by hyperventilation, stating the time but not the rate. Lachmann (1941) in a detailed study of the subject considered hyperventilation a reliable means of revealing latent tetany, even more reliable than Trousseau's phenomenon, but his report did not mention controls. My first attempt (O'Donovan, 1943, 1945) to use hyperventilation consisted in getting the subject to breathe at the rate of 55 to 60 a minute for three minutes. If no tetanic manifestation appeared by then latent tetany was ruled out. In 72 normal adult controls it was observed that only 9 developed carpal cramp at or before three minutes.

This procedure has little practical value, as patients are likely to develop disturbing generalized signs and symptoms after hyperventilation for two or more minutes. Usually it is also found positive only when the tourniquet test is already positive, therefore no further information is gained. In only 7 out of 64 instances of hypocalcaemia did it indicate latent tetany when the tourniquet test was negative. Details are given in the previous publications (O'Donovan, 1943, 1945).

The Combined Test

Hyperventilation was found to be more practical in application if it was used only when the tourniquet test was negative and if begun immediately after release of the tourniquet. It can then very readily produce an isolated cramp in the ischaemic hand. The combination of the two procedures is referred to as the combined test, and the details are as follows.

The tourniquet is applied as described above for four minutes and if no definite carpal cramp appears it is removed and the subject is asked to breathe in and out deeply at 55–60 respirations a minute. He should be sitting upright, with the hands

*Assisted by a grant-in-aid from the Medical Research Council of Ireland.

placed loosely on the knees. The rate may be controlled by using rhythmic pressure on a shoulder with one hand while beating the time with the other. Respirations should flow evenly from expiration into inspiration without pause and should not be unduly forcible. The hyperventilation should be started within 15 seconds after releasing the tourniquet, and the procedure should therefore be explained to the patient before the tourniquet is released. Hyperventilation is stopped at 75 seconds or sooner if carpal cramp appears. In cases of latent tetany the hand previously under the tourniquet becomes spastic before 75 seconds, while there are few or no generalized symptoms of tetany. Rarely the opposite hand becomes cramped also, but not so intensively.

The standard of 75 seconds' hyperventilation is an approximation based upon 68 observations on adults and adolescents of all ages, including 25 female medical students. The same standard is used for both sexes, except that men are asked to hyperventilate more actively. Female medical students are always more sensitive subjects for the demonstration of latent tetany, partly because they tend to carry out the test with excessive enthusiasm and partly because young educated adults are more emotional than the average hospital patient. Hence some normal individuals of this type may reveal tetany even in 60 secs. This variation in the normal control is a disadvantage which is inherent in all tests for mild degrees of latent tetany, and the important characteristic of any test is that it should be positive in a high percentage of hypocalcaemic patients and in only a very small percentage of normal subjects. A positive test then indicates the necessity for a more detailed investigation of the possible causes of tetany.

Four out of the 68 controls developed cramp before or at 75 sec., whilst in 27 observations on 13 patients there were 23 positive reactions. In 58 observations based on Trousseau's sign, and the combined test where necessary, failure to diagnose latent tetany occurred in only three (95% positive) (see Table).

Evaluation of the Combined Test

The combined test is a useful procedure to demonstrate the phenomenon of carpal spasm to applied physiology classes. It shows that tetany is often a summation of factors which increase the sensitivity of the nervous system. In this case alkalosis and the hyperexcitability in the arm are augmenting one another. The test is of some practical value in checking the efficacy of treatment in chronic hypocalcaemic patients who have hypoparathyroidism or steatorrhoea, as it obviates repeated blood analysis. In the individual patient on routine examination the error of variable degrees of hyperventilation is negligible, so that one can very readily detect a sudden drop in serum calcium. Finally, by improving bedside diagnosis the test should aid in the diagnosis of various diseases associated with latent tetany.

The combined test is an improvement on the simple hyperventilation test because it reduces the period of hyperventilation, eliminates the possibility of an unpleasant generalized tetany, and is more sensitive than either the tourniquet test or the hyperventilation test alone. It also reduces the frequency of the necessity to hyperventilate.

The disadvantages include its failure in cases of respiratory disease such as asthma and emphysema, recurrent laryngeal-nerve paralysis after thyroidectomy, and abdominal tumours which prevent the proper movement of the diaphragm. The scope of the test in pregnancy has not yet been investigated. Lastly, in any serious physical or mental disability and in children under 10 years it would be difficult to obtain the necessary co-operation. These points are serious deficiencies in the routine use of the test. There were 4 patients in a total of 34 who were unable to hyperventilate. In two of these Trousseau's sign was already positive, and therefore hyperventilation was not necessary.

Influence of Calciferol

In the initial phase of this investigation it was observed that when hypocalcaemic patients were taking calciferol (50,000 to 150,000 units daily) the tests for latent tetany were frequently negative although the serum calcium was still subnormal. Fig. 1 shows that this inhibitory action of calciferol on latent tetany cannot be entirely attributed to its effect on the serum calcium level. The data in Fig. 1 were obtained by use of Trousseau's sign followed by hyperventilation when Trousseau's sign was negative. As already stated, in 58 observations on hypocalcaemic patients,

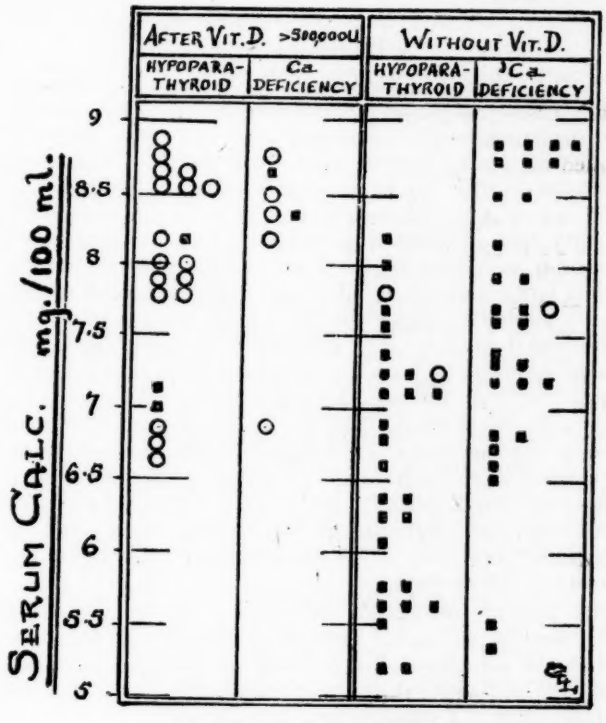

FIG. 1

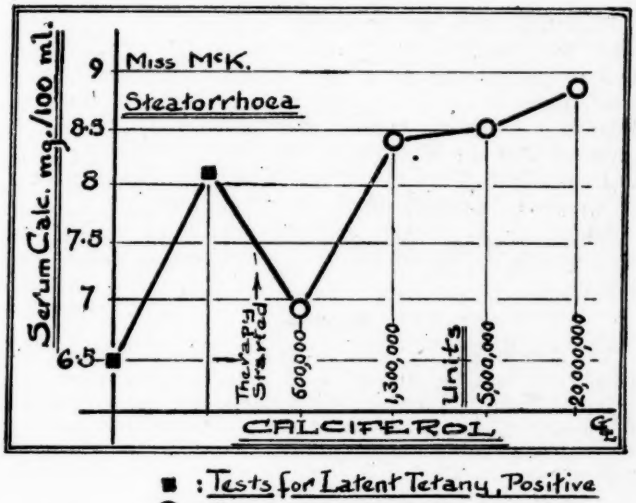

FIG. 2

not taking calciferol, latent tetany was demonstrated in all but three instances. In 27 observations on patients who, notwithstanding calciferol treatment, still had hypocalcaemia the state of latent tetany was demonstrated in only five instances. Calciferol seems to have this effect irrespective of whether the patients have hypoparathyroidism or calcium deficiency. Study of individual patients clearly reveals the effect of calciferol (see Fig. 2).

Discussion

What should be the clinician's criterion of dosage when treating chronic hypocalcaemia with calciferol? The drug appears to influence latent tetany both by raising the serum calcium and by some other independent effect. The doses required to inhibit the signs of latent tetany in the average case of hypoparathyroidism on ordinary diet is between 50,000 and 150,000 units daily. The dose necessary to keep the serum calcium within normal limits may be considerably larger. It would appear more reasonable to base the therapeutic dosage on a biological test than on a purely chemical estimation. The higher dosage necessary to keep the serum calcium around 10 mg. per 100 ml. may not only be unnecessary but may have a deleterious effect on the patient. It seems well established both in animals and in man that the toxic manifestations of vitamin D are not necessarily accompanied by hypercalcaemia (Reed, Struck, and Steck, 1939); while Eaton (1946) reported a hypoparathyroid patient taking calciferol who, notwithstanding a normal serum calcium developed metastatic calcification.

The patients considered here, whose dosage and treatment were based on the signs of latent tetany, have so far shown no ill effect of low blood calcium such as lens opacities. The period of observation, however, is not long enough to permit conclusions.

It is difficult to explain the inhibitory action of calciferol on latent tetany that is not due to increased serum calcium. A relative increase in ionized calcium is at least a theoretical possibility. Unfortunately, complete data on serum protein are not available, but in a small number of cases studied there was no appreciable change. Feeny, Sandiland, and Franklin (1947) found no change in the serum protein fractions, except a slight alteration of globulin fractions, in cases of lupus vulgaris receiving large doses of calciferol. Ingram, Anning, and Dawson (1948) recently reported that the high dosage of calciferol used in treatment of lupus vulgaris did not alter the ionized calcium fraction but significantly increased a diffusible calcium complex. It is unlikely that this alteration would have any bearing on the inhibition of latent tetany as described above.

Summary

The clinical tests for detection of latent tetany in adults and adolescents were investigated, using hypocalcaemia as an index of latent tetany. Almost all the patients observed had *chronic* latent tetany. It was concluded that the well-known tests are unreliable. The tourniquet test was negative in 34% of 89 observations on 32 patients and Chvostek's sign was negative in 73% of observations.

A new test combining the tourniquet test and hyperventilation is described. It is used when the tourniquet test is negative, and is more reliable than either of the two procedures used separately. Of 58 observations on 32 patients 95% were positive. Two other patients whose tourniquet test was negative were physically unable to hyperventilate.

Calciferol has an inhibitory effect on the signs of latent tetany which is independent of the increase in serum calcium. In 22 of 27 observations on patients who had received a total of more than 500,000 units the signs of latent tetany were negatived although the serum calcium was still less than 9 mg. per 100 ml. Calciferol therefore inhibits latent tetany in two ways. The significance of this observation in the treatment of chronic latent tetany is discussed.

References

Clark, E. P., and Collip, J. B. (1925). *J. biol. Chem.*, **63**, 461.
Eaton, J. C. (1946). *Biochem. J.*, **40**, lii.
Feeny, P. J., Sandiland, E. L., and Franklin, L. M. (1947). *Lancet*, **1**, 438.
Ingram, J. T., Anning, S. T., and Dawson, J. (1948). *Brit. J. Derm. Syph.*, **60**, 159.
Lachmann, A. (1941). *Acta med. scand., Suppl.*, **121**, 64.
O'Donovan, D. K. (1943). *Irish J. med. Sci.*, **6S**, 519.
—— (1945). Ibid., **6S**, 146.
Reed, C. I., Struck, H. C., and Steck, I. E. (1939). *Vitamin D.* Chicago.

PATHOGENIC STAPHYLOCOCCI

DETECTION OF α-LYSIN PRODUCTION ON RABBIT- AND SHEEP-BLOOD-AGAR PLATES

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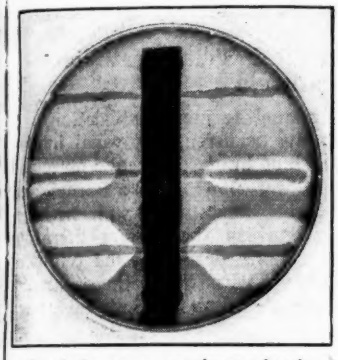
The coagulase reaction is the simplest and perhaps the most important test for pathogenicity of the staphylococcus. However, the agreement between pathogenicity and this reaction, although close, is not absolute (Christie, North, and Parkin, 1946), and it is sometimes desirable to use confirmatory tests. This is especially the case when detecting carriers of pathogenic staphylococci. Christie and his co-workers (1946), having examined a very large number of strains, conclude that the production of α-lysin is the property most closely associated with pathogenicity. This conclusion is shared by Schwabacher *et al.* (1945).

Until recently it was commonly believed that the lysis of a blood-agar plate was an unreliable guide to pathogenicity. The relatively tedious detection of α-lysin in supernatants from broth cultures is still often recommended (Knott, 1947). However, several workers have used sheep-blood-agar plates successfully for this purpose. The changes produced by α- and β-lysins on this medium can usually be distinguished with ease (Naidu, 1934; Bryce and Rountree, 1936; Kojima and Kodama, 1939; Christie and North, 1941). Christie, North, and Parkin (1946), using spot inoculation of strains on sheep-blood-agar plates, observed that with nearly all haemolytic strains there was no difficulty in deciding whether they produced α- or β-lysin. However, with strains producing only a trace of lysis on blood agar it was difficult to decide whether this was due to α-lysin or to something else. Williams and Harper (1947) describe a sheep-blood-plate method similar to that of Christie and his co-workers, except that a control plate containing incorporated α-antitoxin is included with each batch of tests, which are incubated in an atmosphere containing 30% CO_2. They found that the method, although reliable, failed to detect about 2% of α-toxigenic strains (positive by broth method) and that β-lysin, when produced, could mask the α-lysin. They recommend that all apparently negative and all evidently β-toxigenic strains should be tested in a tube before being classed as non-α-toxigenic.

The rabbit-blood-plate method of α-lysin detection described here is simple to perform and gives results which are easily interpreted. Other lysins do not interfere with the test.

Method

Two per cent. rabbit-blood–agar plates are used. The blood is obtained with reasonable aseptic precautions from an ear vein. The strain to be tested is streaked with a loop across the surface of the plate, previously dried in the incubator. Three or four strains can be tested on one 3½-in. (8.75-cm.) plate. The number may be doubled by inoculating different strains on opposite halves of the plate. A strip of sterilized filter-paper about ½ in. (1.25 cm.) wide and containing dried α-antitoxin is laid on the agar at right angles to the inoculation streaks. These papers are prepared by dipping dry-sterilized strips into α-antitoxin (Burroughs Wellcome refined staphylococcus antitoxin, 1,250 units per ml.). The papers are then dried in a Petri dish containing heated plaster-of-Paris and preserved, sealed in a similar dish, in the freezing chamber of an ordinary refrigerator. The method used is that described by Morley (1945) for penicillin-containing test papers. Sufficient papers for many tests may be prepared at one time. They retain their potency unimpaired for at least two months. We have not tested them after longer periods. Their content of dried serum renders the papers somewhat stiff, but when applied closely to the agar they quickly absorb moisture and adhere to its surface.



Staphylococcus α-toxin production on rabbit-blood–agar plate. One negative and two positive strains.

Antitoxin papers may be prepared as required, without drying, by soaking in antitoxin and then blotting briefly. Excess fluid must be avoided, as it may allow the separate strains to run together along the strip when incubated.

The plates are incubated in an atmosphere containing approximately 30% CO_2. After 24 hours most of the positive strains give easily read results. If an apparently negative strain is present the plate is incubated similarly for a further 24 hours before the final reading. Strains which do not produce α-toxin give either no lysis or, more often, a sharply bordered zone of lysis the edge of which is parallel to the growth and which extends right up to the edge of the filter-paper. On the other hand, an α-toxigenic strain shows a wide zone of lysis with hazy margins. Near the filter-paper this zone tapers in the form of a spear-head pointing towards the paper (see illustration). This spear-head zone of narrowing, diagnostic of α-toxigenic strains, is sharply defined by remarkably straight borders corresponding to lines of toxin-antitoxin neutralization. In addition, it is often possible to see straight white lines extending outwards at an angle from the filter-paper. These lines correspond closely with the borders of the haemolysed zone, and are apparently formed by toxin-antitoxin precipitation in zones where optimal proportions exist (Elek, 1948). The presence of other lysins in addition to α-toxin makes no difference to the clarity of the result.

Identical appearances are obtained by spreading antitoxin (4 drops) over half a previously dried plate. The plate is dried again, and strains are then streaked across it at right angles to the dividing line between treated and untreated agar. The necessity for a second drying of the plate renders this technique less convenient than the filter-paper method.

Results

Using this method we examined 201 unselected pure strains of staphylococcus freshly isolated from routine hospital specimens over a period of eight months. The strains were all tested at the same time for α-toxin production in broth (Gillespie, Devenish, and Cowan, 1939) and for coagulase production (Gillespie, 1943). The results obtained are shown in the Table.

Table showing Coagulase Reactions and α-Toxin Production by 201 Strains of Staphylococcus

Rabbit-Blood–Plate Test	α-Toxin in Broth		Coagulase	
	Positive	Negative	Positive	Negative
162 α-toxin-positive strains ..	162	Nil	162	Nil
39 α-toxin-negative strains ..	1	38	6	33

On purely clinical grounds it was impossible to be certain of the pathogenicity of the majority of the staphylococci examined. However, 37 strains were certainly pathogenic for man (isolated from pus from previously unopened, non-contaminated abscesses, films of which showed clusters of Gram-positive cocci only and which yielded pure cultures of staphylococcus). Of these 37 certainly pathogenic strains 36 were positive by both plate and broth test and 37 were coagulase-positive. Evidently the correlation between pathogenicity and α-toxin production on plates is close.

Plate methods of detecting α-toxin production are much more simple to perform than the broth method. In addition, the interpretation of the results of the latter is sometimes rendered difficult by haemolysis occurring rapidly in the control tube (due to lysins other than α-toxin).

Sheep-Blood–Agar Plates.—We have used the filter-paper-strip method on sheep-blood plates in parallel with rabbit-blood plates in testing 33 strains (20 α-toxin-positive and 13 negative). Identical results were obtained in this small series. The specific spear-head zone of lysis is as clear as with rabbit blood, but presumably there is a danger that small amounts of α-lysin may be obscured by β-lysin if sheep blood is used (Williams and Harper, 1947).

Summary

A plate method of detecting staphylococcus α-toxin production is described. Filter-paper strips containing α-antitoxin are used on 2% rabbit-blood–agar plates incubated in an atmosphere containing 30% CO_2. The interaction of the toxin and antitoxin diffusing into the agar at right angles to one another causes a sharp tapering of the wide zone of lysis surrounding α-toxigenic strains. This appearance is specific for such strains.

The test is easy to perform and to interpret, and the results have shown a close correlation with tube α-toxin tests, coagulase production, and the clinical pathogenicity of the strains examined.

References

Bryce, L. M., and Rountree, P. M. (1946). *J. Path. Bact.*, **43**, 173.
Christie, R., and North, E. A. (1941). *Aust. J. exp. Biol. med. Sci.*, **19**, 323.
—— —— and Parkin, B. J. (1946). Ibid., **24**, 73.
Elek, S. D. (1948). *British Medical Journal*, **1**, 493.
Gillespie, E. H. (1943). *Bull. Emerg. Publ. Hlth Lab. Serv.*, **2**, 19.
—— Devenish, E. A., and Cowan, S. T. (1939). *Lancet*, **2**, 870.
Knott, F. A. (1947). In Dyke's *Recent Advances in Clinical Pathology*. Churchill, London.
Kojima, T., and Kodama, T. (1939). *Kitasato Arch.*, **16**, 197.
Morley, D. C. (1945). *J. Path. Bact.*, **57**, 379.
Naidu, P. M. N. (1934). *Zbl. Bakt.*, **132**, 47.
Schwabacher, H., Cunliffe, A. C., Williams, R. E. O., and Harper, G. J. (1945). *Brit. J. exp. Path.*, **26**, 124.
Williams, R. E. O., and Harper, G. J. (1947). *J. Path. Bact.*, **59**, 69.

A CASE OF DICOUMAROL POISONING

BY

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The following case emphasizes the grave danger of the use of the anticoagulant dicoumarol without adequate laboratory control. It also stresses the importance of the use of fresh blood and not stored blood in the therapeutic control of haemorrhage from dicoumarol overdosage. Vitamin K and stored blood are without effect. There is a definite latent period before therapeutic measures can take effect, and various mechanical factors may have to be dealt with. The reaction to treatment, when it occurs, is dramatic, and no case can be considered hopeless. In this instance, despite the severe and generalized nature of the haemorrhages, complete recovery occurred.

Case Report

The patient, a man aged 57, was admitted to hospital on account of severe haematuria on Oct. 4, 1947. He had read in the daily papers that dicoumarol had been used for coronary thrombosis, but it was not known that the cause of the haematuria was dicoumarol until a detailed history was taken, and by this time various other severe haemorrhagic symptoms were present. It was revealed that on his own initiative he had taken 100 mg. daily for nine or ten days. There was a latent period of seven days before signs and symptoms appeared. This latent period has been previously pointed out by Crawford and Nassim (1944). The first symptom was abdominal pain, which preceded sudden gross haematuria by 24 hours.

Within 24 hours of being admitted to hospital the patient's general condition deteriorated rapidly. Multiple petechial haemorrhages occurred in the skin and subcutaneous tissues, then melaena and a massive sublingual haematoma developed which increased in size hourly. The initial B.P. was 160/115. The tongue became the size of a tangerine orange and immediately threatened to obstruct his airway. Despite the immediate transfusion of blood the swelling of the tongue increased and a tracheotomy was performed while transfusions were continued. A considerable submandibular haematoma developed and the patient was *in extremis*. His B.P. was 90/74 on Oct. 7. The anoxaemia was relieved but haemorrhages continued. A pint (570 ml.) of stored blood was given, with vitamin K injections intramuscularly; the response was not satisfactory, and haemoptyses occurred. *X*-ray examination with a portable apparatus revealed multiple shadows in the lung fields. Further transfusion of 1 pint of fresh blood was given on Oct. 8, but his condition remained precarious. A further 3 pints (1.7 litres) of blood was obtained from the relatives, and this was given by slow drip over the next 48 hours. His condition gradually improved and the haematuria and petechial haemorrhages decreased. Whole-blood transfusion had a dramatic effect on the prothrombin times. These were: Oct. 7, 47% normal; Oct. 8, 48% normal; Oct. 9, 50% normal; Oct. 17, 57% normal.

Examination of the blood on Oct. 5 showed: haemoglobin, 82%; red cells 3,600,000; white cells, 12,200; reticulocytes, 3%; platelets, 108,000. On Oct. 10 the haemoglobin was 50%. On the 14th the white cells numbered 8,000, reticulocytes 7%, platelets 240,000. On the 17th the haemoglobin was 97%; red cells, 4,800,000; white cells, 8,600; reticulocytes, 5%; platelets, 288,000.

Discussion

Dicoumarol must be considered in the differential diagnosis of all cases of haematuria in which the drug has been taken. This is discussed by Rosenbloom and Crane (1946). It would appear that haematuria is one of the earliest signs of dicoumarol intoxication and an indication for correct therapy, as more severe symptoms may quickly supervene in a matter of hours. In our case venesection before transfusion was not performed, as was practised by Shlevin and Lederer (1944), although there was a definite danger of left-sided heart failure from a recent coronary thrombosis. Jaundice developed 130 days after the initial transfusion. This was taken to be of the homologous serum type rather than due to any direct toxic action of the dicoumarol on the liver. Jaundice as a manifestation of dicoumarol poisoning has not yet been reported. The present case, we think, illustrates the importance of including dicoumarol in the list of dangerous drugs.

Grateful thanks are due to Sister B. Coysh for correlation of clinical details, to Mr. F. J. C. Matthews, assistant surgeon, for performing the tracheotomy, to Dr. R. C. Hill, pathologist, and to Mr. F. J. Howe, Hospital of St. Cross.

References

Crawford, T., and Nassim, J. R. (1944). *Lancet*, **2**, 404.
Rosenbloom, D., and Crane, J. J. (1946). *J. Amer. med. Ass.*, **132**, 924.
Shlevin, E. L., and Lederer, M. (1944) *Ann. intern. Med.*, **21**, 332.

Medical Memoranda

Auricular Fibrillation after Trichlorethylene Anaesthesia

The following case is unusual enough to merit publication. It is of interest in that although the occurrence of vagal inhibition (Haworth and Duff, 1943), sinus bradycardia, and auricular and ventricular extrasystoles (Hewer, 1942, 1943; Barnes and Ives, 1944) has been noted during anaesthesia with trichlorethylene, there is only one record in the current literature (Lloyd-Williams and Hewspear, 1942) describing the onset of auricular fibrillation in association with this form of anaesthesia, although by now innumerable administrations have been given in this country alone.

Case History

A healthy woman aged 50 was admitted to hospital for the repair of a large cystocele and rectocele. She had always been in excellent health, and at the pre-operative examination she appeared to be very fit, with no clinical evidence of cardiovascular disease. The blood pressure was 140/90. She was, however, unduly nervous and apprehensive.

Pre-operative medication consisted of 1/6 gr. (11 mg.) of morphine and 1/150 gr. (0.43 mg.) of hyoscine. Anaesthesia was induced with 0.5 g. of sodium thiopentone, and this was followed by nitrous oxide, oxygen, and trichlorethylene, using a "semi-closed" technique with the standard Boyle machine. Induction and maintenance were smooth and uneventful. Anoxia was not permitted at any time, and there were none of the usual signs to indicate overdosage of the drug—which was not surprising, as the absolute minimum was used. No irregularities of the pulse were noted during operation, which lasted 55 minutes. At the end of the operation the patient's general condition was good, but the pulse rate was rather slow (65).

Fifteen minutes later we were called to the ward; she was almost conscious, but sweating profusely and rather pale, with a pulse rate of 40. In the absence of other findings it was considered that this might be a vagal effect and 1/100 gr. (0.65 mg.) of atropine sulphate was given intravenously. Within two minutes the pulse rate had returned to 65–70 and remained so, although from time to time multiple extrasystoles could be detected by palpation and auscultation. Four hours later we were again called to see her and found that she was dyspnoeic and slightly cyanosed, but apart from the dyspnoea she felt quite comfortable. On examination auricular fibrillation was present with ventricular rate of approximately 165. There were no other abnormal clinical signs. A course of intensive "digoxin" therapy was instituted. The following morning auricular fibrillation was still present, but the ventricular rate was down to 100 and the cyanosis and dyspnoea had disappeared. By evening the fibrillation had ceased and the cardiac rhythm was completely regular, the pulse rate being 75. Digoxin was discontinued and the cardiac rhythm remained normal. Further convalescence was uneventful. Unfortunately it was impossible to have an electrocardiogram taken during the period of fibrillation, but clinically the diagnosis was never

doubt. Electrocardiograms taken subsequently showed no abnormality in rhythm or evidence of myocardial disease. There was no evidence of thyrotoxicosis and the blood Wassermann reaction was negative. One month after operation the patient was symptomless and was carrying out her normal household duties.

Comment

The work of Meek, Hathaway, and Orth (1937) and Meek (1940) has provided useful information with regard to the effects of anaesthetic agents on cardiac automaticity. It seems likely that arrhythmias arising below the sino-auricular node are due to vagal stimulation, which causes depression of the sino-auricular node, bradycardia, and the appearance of auricular and ventricular extrasystoles (escape phenomena). Because of this depression of the sino-auricular node the ventricular muscle is rendered more sensitive to stimulation, particularly by adrenaline, and ventricular fibrillation may occur. This is presumably the mechanism of ventricular fibrillation occasionally seen during chloroform anaesthesia. Trichlorethylene is of course very similar to chloroform in chemical composition, and clinical reports bear out this similarity of action, although it is much less toxic and potent. Waters, Orth, and Gillespie (1943), basing their opinion on only a few cases, decided that the drug might have undesirable effects on cardiac automaticity, but up to the present time clinical experience has not really justified this view. In their electrocardiographic investigation of 40 patients undergoing operations under trichlorethylene anaesthesia Barnes and Ives (1944) demonstrated various simple arrhythmias such as sinus bradycardia and auricular and ventricular extrasystoles, but found no evidence of auricular or ventricular fibrillation.

In our case the sequence of events—vagal stimulation with bradycardia, extrasystoles (presumably auricular), and auricular fibrillation—was well demonstrated. Theoretically there would seem to be no reason why auricular fibrillation and not ventricular fibrillation should not follow on multiple auricular extrasystoles in the absence of suitable ventricular stimulation—e.g., excess adrenaline. This case is of further interest in that the cardiac arrhythmias occurred in the immediate post-operative period, when presumably most of the trichlorethylene had been excreted. Adrenaline was not used during operation nor was the patient intubated—factors present in the other recorded case. In view of the patient's state of health both before and after operation it is difficult to dissociate the trichlorethylene anaesthesia and the onset of fibrillation.

It should be noted that the trichlorethylene used in this case was from a newly opened bottle which when subsequently examined conformed to the usual tests of purity. Several patients have since been anaesthetized with trichlorethylene from the same bottle without untoward effect.

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References
Barnes, C. G., and Ives, J. (1944). *Proc. R. Soc. Med.*, **37**, 528.
Haworth, J., and Duff, A. (1943). *British Medical Journal*, **1**, 381.
Hewer, C. L. (1942). *Proc. R. Soc. Med.*, **35**, 463.
— (1943). Ibid., **36**, 463.
Lloyd-Williams, K., and Hewspear, D. (1942). *British Medical Journal*, **2**, 170.
Meek, W. J. (1940). *Proc. Mayo Clin.*, **15**, 237.
— Hathaway, H. R., and Orth, O. S. (1937). *J. Pharmacol.*, **61**, 240.
Waters, R. M., Orth, O. S., and Gillespie, N. A. (1943). *Anesthesiology*, **4**, 1.

An Unusual Trophic Ulcer

Numerous papers have been written on lesions of the lumbar intervertebral disks and their relation to sciatic pain since the pathology was described by Love in 1939. In addition to sciatic pain other conditions have been ascribed to disk lesions. Massive extrusions of the lumbar disks are known to produce cauda equina lesions with severe sphincter disturbances (ver Brugghen, 1945). Pennybacker (personal communication) has seen trophic ulcers complicating cauda equina lesions due to prolapse of the lumbar disks. Burns and Young (1945) attribute the majority of cases of chronic backache to disk lesions.

Search of the extensive literature has failed to reveal any reference to a trophic ulcer of the foot being produced by an old lesion of a lumbar intervertebral disk, and it is thought that the following case is of sufficient interest and importance to merit publication.

The usual causes of trophic ulcers given in neurological textbooks are tabes dorsalis, diabetes, spina bifida occulta, leprosy, and syringomyelia (rarely). As trophic ulcers are not uncommon it is possible that not a few are due to old disk lesions which have been missed because the more usual causes are not common maladies, with the single exception of diabetes. Furthermore, Schmorl (1927) finds prolapse of an intervertebral disk present in 38% of necropsies. Leigh (1947) points out that sensory regeneration may not occur, as compression of the nerve root in disk lesions involves the sensory fibres most of all.

Case Report

A truck-driver aged 29 was referred from the surgical to the medical out-patient department on account of an absent right ankle-jerk. In March, 1947, he was seen in the surgical out-patient department on account of an excavated and discharging ulcer on the plantar surface of his right heel. It was painless and had been present for about 10 weeks. He denied injuring his heel. Excision was advised. A week later he was admitted to a surgical ward, and two days later the ulcer was excised under a general anaesthetic. The wound was packed with vaselined gauze. He was discharged after a week ; a radiograph of the foot taken at this time showed that there was no bony lesion or radio-opaque foreign body in the heel. A week later the ulcer was healing satisfactorily. A section of the ulcer showed "capillary thromboses and haemorrhages in dermal papillae in a portion of horny skin from the heel."

He was seen again on Aug. 11, 1947, when he said that the ulcer had broken down some eight weeks previously, but it was still painless. Further inquiry into his history elicited the following information: In March, 1944, he had had pain in the right side of the back, buttock, and down the back of the thigh and leg to the lateral border of the foot and of the heel ; the pain had lasted 10 weeks and he had been away from work for six weeks. When the pain had subsided it had been replaced by numbness of the outer side of the right foot and heel. There was no history of trauma. At no time had there been any disturbance of micturition.

On examination he was seen to be a healthy-looking man. The only abnormal neurological signs in the legs were an absent right ankle-jerk and marked impairment of pain and touch sensibility over the lateral border of the foot, both dorsal and plantar surfaces of the heel, and of the posterior aspect of the thigh. Flexion of the extended leg at the hip was painless (Lesègue's sign negative). The ulcer measured 1 by 1 cm. and was 0.5 cm. deep; it had a granulated base and undermined edges. The arteries of the right foot were easily palpable. There was some loss of normal lumbar lordosis and flattening between the fifth lumbar spine and the first piece of the sacrum. There was no tenderness anywhere, and movements were full. No other abnormal physical signs were found in the central nervous system. Wassermann and Kahn reactions were negative. Radiographs showed no abnormality of the lumbo-sacral region.

It was not considered justifiable to submit this patient to laminectomy ; his disability was slight, he was at work, and the long history suggested damage to the posterior nerve root which was probably permanent. Accordingly local treatment to the ulcer was intensified.

Discussion

This case well illustrates the following points : (1) The typical sciatic pain in 1944 was replaced by numbness over the lateral side of the foot and heel—a point which is often missed in the history, as the patient pays little attention to numbness compared with the severe pain ; the numbness tends to persist. The length of the history and the absence of progression of symptoms almost certainly exclude a very slowly growing tumour compressing the first sacral nerve root. (2) The abnormal neurological physical signs and flattening of the lower lumbar spine suggest a prolapse of the disk between the fifth lumbar and first sacral vertebrae. These signs tend to persist. (3) The ulcer was no doubt due to the impairment of pain sensibility, which corresponds to the sensory division of the first sacral nerve root ; it was this root which was compressed by the extruded disk. (4) The relation of the sciatic pain three years previously was not correlated with the ulcer of the foot until the question of the absent ankle-jerk presented itself for elucidation.

My thanks are due to Dr. S. A. Propert, honorary physician, and Mr. Ronald Reid, honorary surgeon, Essex County Hospital, Colchester, for their interest and encouragement in the preparation of this report.

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References
Burns, B. H., and Young, R. H. (1945). *Lancet*, **2**, 424.
Leigh, A. D. (1947). *Postgrad. med. J.*, **23**, 141.
Love, J. G. (1939). *Proc. R. Soc. Med.*, **32**, 1697.
Schmorl (1927). *Der Handl. d. deutsch. path. Gesellschaft*, **22**, 250.
ver Brugghen, A. (1945). *Surg. Gynec. Obstet.*, **81**, 269.

Reviews

JUVENILE DELINQUENCY

Juvenile Delinquency in an English Middletown. By Hermann Mannheim. International Library of Sociology and Social Reconstruction. (Pp. 131. 12s. 6d.) London: Kegan Paul, Trench, Trubner and Co. 1948.

The latest addition to the International Library of Sociology and Social Reconstruction is a sociological study of juvenile delinquency on regional lines. The author believes that oecological studies of delinquency afford a promising line of approach, supplementing statistical mass inquiries and prolonged studies of a few individual cases. He describes the nature, causes, and treatment of delinquency in the Borough of Cambridge, and in his task has received valuable information from authorities and officials.

Dr. Mannheim found that during the five years 1941 to 1945 the average figure for indictable offences committed by juveniles in Cambridge was exactly twice the figure given by Dr. E. C. Rhodes for the borough in 1934 to 1936. But in comparison with other localities the increase was not considered to be particularly high. Among many interesting data the fact that some of the new housing estates showed a considerably higher incidence of juvenile delinquency than the town as a whole has some general interest. The author considers that rehousing in itself is no panacea for social evils unless accompanied by social services such as youth centres and other measures which deal with some of the needs of a youthful community. In the absence of statistical data Dr. Mannheim was unable to accept the suggestion that the cause of the delinquency was attributable to a greater number of children in the families than in other wards.

While stressing the need for further research into juvenile delinquency by persons not engaged in the treatment of offenders, Dr. Mannheim believes that such studies should be supplemented by those of probation officers, institutions for juvenile delinquents, and child-guidance clinics. The data collected are instructive, and the recommendations on the administration of juvenile courts are provocative. The book is written with the author's usual lucidity and is a welcome addition to the increasing literature on the subject.

W. NORWOOD EAST.

ORAL IMMUNIZATION

Oral Vaccines and Immunization by Other Unusual Routes. By David Thomson, O.B.E., M.B., Ch.B., D.P.H., and Robert Thomson, M.B., Ch.B. Assisted by James Todd Morrison, M.D., D.P.H. (Pp. 329; £2 2s.) Edinburgh: E. and S. Livingstone. 1948.

This monograph is in the main a review of the literature, over 1,000 papers being quoted, and in part an account of the authors' own experiences. They begin by declaring their belief that immunity can be obtained by vaccines administered orally, or by inunction, spraying into the nose or trachea, or instillation into the conjunctival sac. They grant that the results are less certain and that much more frequent repetition is necessary than when the parenteral route is used, but unpleasant reactions are obviated and what may be called needle resistance is circumvented. They review very fully the literature on oral vaccination against enteric fever and dysentery, the most logical and best-supported example of this method. They also give a long account of oral B.C.G., although this form of vaccination differs radically in principle from the others considered in that the vaccine is a living one; even so, it is noteworthy that the oral administration of B.C.G. has now been superseded. From these and other more or less reasonable subjects the authors descend to discussing with apparent seriousness such unscientific practices as treating diphtheria with oral antitoxin, ulcerative colitis with an oral Bargen's coccus vaccine, and pyorrhoea with a vaccine-containing toothpaste. If the authors write from too credulous a standpoint for us always to respect their conclusions, we must nevertheless be grateful to them for a guide to the literature of an obscure and interesting subject.

L. P. GARROD.

PEPTIC ULCERATION

Ulcer of the Stomach, Duodenum and Jejunum. By Ralph C. Brown, M.D. Edited by Henry A. Christian, M.D., Sc.D., F.A.C.P., F.R.C.P.(Can.). (Reprinted from the Oxford Loose-Leaf Medicine with the same page numbers as in that work.) Oxford Medical Publications. (Pp. 108; illustrated. 12s. 6d.) New York and London: Oxford University Press (Geoffrey Cumberlege).

This small book is a reprint of the chapters on peptic ulceration in the *Oxford Loose-Leaf Medicine.* It is a concise but complete account of the modern view of the subject. The author was a pupil of Sippy's, and for many years has himself been in charge of the clinic at the Presbyterian Hospital in Chicago, where Sippy worked. The book therefore not only has an authoritative air but is at all times very practical.

To cover the whole subject in a little more than 100 pages considerable condensation has been necessary, and in order to produce a balanced narrative the author draws fully on his own experience. Nevertheless some gaps must occur, and the author gives an account of some procedures not in general use but which no doubt are most successful in his hands. Thus he makes the clinical differentiation between peptic ulcer and gall-bladder disease and functional dyspepsia sound very simple. Similarly, in the treatment of severe haematemesis when it is thought that bleeding is continuing he advocates gastric lavage with ice-cold water followed by 15 ml. of adrenaline by mouth. There is a good bibliography and the book is well illustrated by tracings from radiographs.

CHRISTOPHER HARDWICK.

STATE MEDICINE IN ENGLAND

The History of State Medicine in England. Being the FitzPatrick Lectures of the Royal College of Physicians of London for the years 1946 and 1947. By Sir Arthur S. MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S. (Pp. 82. 12s. 6d.) London: Royal Institute of Public Health and Hygiene.

Most of this book is occupied by the FitzPatrick Lectures given at the Royal College of Physicians in 1946 and 1947, which deal with the period from the accession of Victoria to the establishment of the Ministry of Health in 1919. But the author has greatly improved the book by including the lecture on the "Evolution of Preventive Medicine in England" given at the Royal Society of Medicine in 1946. Thus he has concisely covered the whole ground. His account is no dry summary, for it is lit up by many attractive biographies of the persons chiefly concerned, particularly those who inspired progress in the late 'nineties and in the present century. While paying his due meed of praise to the early pioneers, Sir Arthur claims that Southwood Smith, Arnott, and Kay "were the medical architects, and Edwin Chadwick the actual builder of the edifice." His sidelights on the personalities of the men with whom he was personally familiar, such as Horsley, Klein, Thorne Thorne, Downes, Monckton Copeman, and Newsholme, are illuminating. His generous reference to James Kerr, whose pioneer work in school welfare is apt to be forgotten, is well deserved. The book is copiously documented, written in an easy, attractive style, and is a useful epitome of how a system grew up in which the author has taken an active part. The publishers deserve commendation for the attractive appearance of the book.

ALFRED COX.

A PSYCHIATRIC SYNTHESIS

Psychiatry. A Short Treatise. By William A. O'Connor, L.M.S.S.A., D.P.M. (Pp. 380. 35s.) Bristol: John Wright and Sons. 1948.

This is a short textbook of psychiatry for students of psychiatry, and is not suitable for use as a reference book or as a text for unqualified students. It is interesting for the attempt the author makes to combine psycho-analytic doctrine with a classical nosology. The two do not, unfortunately, combine at all well. The author himself feels that it is "a far cry from the basement membrane of the testis to the meta-psychological theorizings of the psycho-analysts." The book is full of such asides. Discussing the sometimes pleasurable tone of very mild anxiety feelings, he remarks: "Is it then true to say that in the midst of a life-giving process we feel the threat of dissolution? Or is it nearer the truth to suppose that in the midst of satisfying a biological need we fear lest the ultimate orgasm fail us?"

There is an unfortunate emphasis on body–mind dualism. The somatic aspects of schizophrenia are to be seen only in its "strange and inexplicable" physical symptoms. Behaviour becomes understandable when described by far-fetched analogies—e.g., he describes psychoses as anaphylactic phenomena, sensitization having been produced by repeated psychic shocks. Preclinically, physical disease is an unconscious process. One may expect to find psychic symptoms of the presence of schizophrenia in early childhood. The author's point of view is a highly individual one. Nevertheless there is much of interest. He describes the historical development of psychiatric concepts at greater length than is usual, and though his account will probably not help the student much it will interest the psychiatrist. His discussion of the more important recent advances, including physiological and genetical studies as well as psycho-analytical, is for the most part adequate. Even though it seems quite unsuccessful to the reviewer, a synthesis has been attempted; and the writing is both lucid and fresh.

ELIOT SLATER.

DENTAL DISEASE AND PATHOLOGY

Oral and Dental Diseases. By Hubert H. Stones, M.D., M.D.S., F.D.S.R.C.S.Eng. (Pp. 896; 926 illustrations, 82 in colour. £4 10s.) Edinburgh: E. and S. Livingstone, Ltd.

Surgical Pathology of the Mouth. By E. Wilfred Fish, C.B.E., M.D., Ch.B., L.D.S.(Manch.), D.D.Sc.(Melb.), D.Sc.(Lond.), F.D.S.R.C.S.(Eng.). (Pp. 463; 236 figures. 50s.) London: Sir Isaac Pitman & Sons, Ltd.

It is a coincidence that two such excellent books should have been produced at the same time, when a want for them has been felt for many years. Both books are very well produced and illustrated, and while Professor Stones covers a wider field Dr. Fish has selected certain aspects of oral and dental pathology which he discusses in detail; the former is more impersonal and the latter more personal. The information in both books is up to date, and the references at the end of each chapter in *Oral and Dental Diseases* make it easy for the reader to find more on any subject. Dr. Fish describes the pathology underlying many surgical procedures, and the book is in fact largely founded on experimental work.

The books are complementary to each other. Professor Stones's should be very useful to both student and practitioner for information and reference. Dr. Fish's is more about the pathology of certain clinical conditions, and should equally certainly be read by student and practitioner.

ALEXANDER MACGREGOR.

We receive again—perhaps for the last time, but we hope not—*The Hospitals Year-Book, 1947*, edited by J. P. Wetenhall (The British Hospitals Association, 21s.). It is a useful directory listing all the hospitals in Great Britain and Ireland, local authority as well as voluntary. A new feature this year is a list of hospitals providing rehabilitation services. There are between 300 and 400, though in some cases the organization is still meagre. The editor gives some forecast of hospitals in the new National Health Service, but he points out that the Act, "with a frequency unparalleled in former legislation," relegates every aspect of administration to be dealt with in future regulations and orders. Yet it is the administration, not the Act itself, which will determine whether the new Service is good, bad, or indifferent. He points out also the dangers of standardization—a word with a double meaning, connoting perhaps the creation of standards of quality, design, and manufacture, or perhaps only a dead level of mediocrity. It might be thought that in a nationally organized hospital service economy and enhanced efficiency are to be expected owing to central buying of supplies and uniformity of equipment; but Mr. Wetenhall shows that these methods, while they have their value, will not necessarily do all that is expected of them, especially if they are indiscriminately or excessively used. Discussing the medical staff, he urges the importance of a medical committee at each hospital in close contact with the house or management committee. The internal administration of the hospital must be such as to ensure professional freedom in the treatment of patients and the prosecution of research. It is hinted that this may be the last issue of the year-book, for it is published under the auspices and at the expense of the British Hospitals Association, which can no longer exercise a representative function on behalf of voluntary hospitals once such hospitals have lost their voluntary status. But the new era in hospital administration will be at a disadvantage if it is deprived of what Mr. Bevan himself in a foreword calls "an institution in the hospital world," and it is to be hoped that in some form or other it will be continued.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

The Surgery of the Stomach and Duodenum. By T. H. Somervell, M.A., M.B., B.Ch., F.R.C.S. (Pp. 546. 45s.) London: Edward Arnold. 1948.

Includes detailed descriptions, with illustrations by the author, of operative methods.

Biology of Disease. By Eli Moschcowitz, M.D. (Pp. 221. $4.50.) New York: Grune and Stratton. 1948.

Essays on the aetiology and pathology of a number of diseases.

The Pathologic Physiology of Uremia in Chronic Bright's Disease. By S. E. Bradley, M.D. (Pp. 69. 10s. 6d.) Oxford: Blackwell Scientific Publications. 1948.

The author relates the functional disorders of various organs to the clinical manifestations of uraemia.

Medical Hypnosis. By L. R. Wolberg, M.D. Vol. 1. (Pp. 449. $5.50.) Vol. 2. (Pp. 513. $6.50.) New York: Grune and Stratton. 1948.

The use of hypnosis in psychotherapy.

Co-operation, Tolerance, and Prejudice. By S. Lowy, M.D. (Pp. 318. 21s.) London: Routledge and Kegan Paul. 1948.

The sociology and psychology of intolerance and prejudice.

Malleus Maleficarum. Translated by the Rev. Montague Summers. (Pp. 278. 15s.) London: Pushkin. 1948.

The first translation into English of this famous work on the extermination of witches.

Radiotherapy and Cancer. By A. G. C. Taylor, M.R.C.S., L.R.C.P., D.R., F.F.R., and others. (Pp. 81. 7s. 6d.) London: H. K. Lewis. 1948.

A summarized account based on the authors' experience.

Essentials of Pathology. By L. W. Smith, M.D., F.C.A.P., and E. S. Gault, M.D., F.C.A.P. 3rd ed. (Pp. 764. $12.00.) Philadelphia: Blakiston Company. 1948.

A textbook for medical students.

Kleine Chirurgie. By Hans Kurtzahn, revised by W. Heyn. 12th ed. (Pp. 496. M. 17.50.) Berlin: Urban and Schwarzenberg. 1948.

A short textbook of surgery.

Wetter und Krankheiten. By H. Berg. (Pp. 140. M. 6.50.) Bonn: H. Bouvier. 1948.

An account of the relation between climate and disease.

Die Immunitätsforschung. Die Antigene. By R. Doerr. Vol. 3. (Pp. 375. No price.) Vienna: Springer. 1948.

A monograph on research into antigens.

The Diabetic A B C. By R. D. Lawrence, M.A., M.D., F.R.C.P. 10th ed. (Pp. 80. 4s.) London: H. K. Lewis. 1948.

Instructions for the diabetic patient.

Le Foie Vasculaire. By M. Favre. (Pp. 98. 220 francs.) Paris: Masson. 1948.

A monograph on hepatic cirrhosis.

Traité de Médecine. Edited by A. Lemierre, and others. Vol. 7. (Pp. 1063. 2,300 francs.) Paris: Masson. 1948.

This volume is on the alimentary system.

Modern Trends in Psychological Medicine 1948. Edited by N. G. Harris, M.D., F.R.C.P., D.P.M. (Pp. 450. 50s.) London: Butterworth. 1948.

Contributions by various authorities.

Conception Physique de la Vie. By D. Calewaert. 2nd ed. (Pp. 234. No price.) Paris: Librairie Maloine. 1948.

The author describes his theory of density and tensions in living organisms.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 20 1948

SPONTANEOUS PNEUMOTHORAX

Since Kjaergaard[1] published his careful studies non-tuberculous spontaneous pneumothorax has been easy to recognize clinically, and it is not usually difficult to distinguish between it and spontaneous pneumothorax occurring as a result of pulmonary tuberculosis. Simple non-tuberculous pneumothorax is characterized by absence of previous symptoms of disease, afebrile course, normal sedimentation rate, absence of pleural exudate, uneventful re-expansion of the lung in most cases, and failure to find radiological evidence of pulmonary disease in the re-expanded lung. Cases are relatively rare in which doubt remains whether the condition is tuberculous or non-tuberculous after consideration of all these factors, and the treatment of the majority of cases of simple spontaneous pneumothorax presents no difficulty. Some patients are liable to recurrent attacks, and the occasional case in which the lung fails to re-expand and the pneumothorax becomes chronic presents a special, though rare, problem.

The mechanism responsible for simple spontaneous pneumothorax, especially the chronic and recurrent types, has not been thoroughly investigated, though isolated cases showing cystic and bullous emphysematous changes of various sorts have been reported and valvular mechanisms have been demonstrated histologically.[2 3] The publication by R. C. Brock[4] of his observations on 71 cases of recurrent and chronic spontaneous pneumothorax is therefore most informative and welcome. He defines chronic pneumothorax as one which has failed to re-expand after three months; there were 45 of these cases, 17 of which became chronic after recurrent attacks. The average duration was 15 months and the longest 9½ years. The recurrent group consisted of 25 cases (excluding the 17 which became chronic). Fifteen of the recurrent cases had alternating bilateral attacks, and in 8 both lungs became collapsed simultaneously. The teaching of Kjaergaard and others about non-tuberculous spontaneous pneumothorax does not yet seem to be widely enough known, since Brock remarks that many of his patients had wasted time undergoing sanatorium treatment. The ages of his patients ranged from 1¼ years to 64 years. The age distribution within this range differed from that in the series of 358 cases of simple pneumothorax collected by Perry,[5] since in his series the condition developed most frequently in the third decade, whereas in Brock's series of recurrent and chronic cases the greatest incidence was spread over the third, fourth, and fifth decades. This difference was probably due to the greater number of cases with gross emphysematous changes in Brock's series.

In only one of Brock's cases was tuberculosis found to be the cause. In one case the pneumothorax had produced no symptoms and was discovered accidentally, and in others a small pneumothorax was found on the opposite side to that which was being investigated. In the severe cases of chronic pneumothorax there was often great loss of weight, which was regained after the lung had been induced to re-expand. Ordinary radiographic examination may show nothing more than the pneumothorax, though emphysema may be seen in the opposite lung. It may be difficult to distinguish between pneumothorax and a giant cyst or bulla, but it is of practical importance, since needling a bulla in the mistaken belief that it is a pneumothorax may result in a tension pneumothorax if the pleura is free, and this can produce severe symptoms or even be fatal. Tomography or bronchography may help to differentiate the two conditions. If it is thought advisable to needle a patient before it is known for certain whether the condition is a bulla under tension or a pneumothorax preparations should be made for the treatment of tension pneumothorax if necessary, or even for the performance of thoracotomy. Intrapleural pressure readings are valuable in demonstrating conclusively the presence of a fistula, which is shown by a rapid return of the pressure to the previous reading after withdrawal of air. Thoracoscopy is the most valuable examination and should never be omitted.

Brock was able to find the probable cause of the condition in all except six of his seventy-one cases; in these six no cause was discovered even after the most exhaustive investigation. Emphysema was present in 25 cases, in 13 of which it was classified as bullous; 8 patients also had asthma and bronchitis. In 11 cases there were large solitary bullae or cysts; in three diffuse polycystic disease; in 15 small bullae, mostly apical; and in six an apical scar. The actual leak or tear was seen through the thoracoscope in four cases. An interesting observation is the appearance of areas resembling "cuckoo spit." In three of the patients in whom it was found emphysema was also present, but in the fourth there was no other evidence of abnormality in the lungs. The area is made up of a number of scattered foci on the pleura consisting of a few tiny air bubbles each less than a millimetre in diameter. When the patient was instructed to make expiratory efforts with the nose held these clusters of air bubbles became larger and the number of bubbles increased. Brock suggests that these foci can probably disappear and reappear in different places, and this would explain why no abnormality has been found at post-mortem examination in the lungs of some patients dying with spontaneous pneumothorax. He considers that in these cases there is a defect of quality, presumably congenital but possibly acquired, which makes the pleura liable to leak or rupture easily. In one case he observed rupture of the pleura during a thoracoscopy when a swab-holder slipped and fell gently on to the lung. Brock's conclusion is that there are several conditions which may cause chronic and recurrent spontaneous pneumothorax. It may arise in the pleura from tearing at the site of an adhesion or from defective quality of the pleura itself; it may be subpleural from bullae, either in connexion with old scars or with

[1] *Acta med. scand., Suppl.*, 1932, **43**.
[2] Hayashi, J., *Frankfurt. Z. Path.*, 1915, **16**, 1.
[3] Fischer, B., *Z. klin. Med.*, 1922, **95**, 1.
[4] *Thorax*, 1948, **3**, 88.
[5] *Quart. J. Med.*, 1939, **8**, 1.
[6] *J. thorac. Surg.*, 1935, **4**, 251.

emphysema, and possibly from congenital maldevelopment of alveoli; it may lie in generalized changes in the alveoli in the form of emphysema; or it may be in the bronchioles or bronchi as in congenital or acquired cystic conditions.

Treatment depends on the cause. If the condition is due to large localized cysts or bullae (such cases are in the minority) the correct treatment is excision, either by lobectomy or local resection. Brock treated eight of his patients in this way. If a localized cystic condition is not present treatment in most of the remaining cases should be by obliteration of the pleura (pleurodesis) by a chemical pleurisy. Brock prefers silver nitrate solution for this purpose; a 20% solution may be swabbed on to the pleura at thoracoscopy or 5–10 minims (0.3–0.6 ml.) of a 10% solution can be injected with an all-glass syringe. In either case it is important to aspirate air immediately after the treatment in order to get the pleural surfaces into apposition while they are inflamed. More than one injection may be required. This procedure gives rise to a reaction which may be severe, with pain and fever up to 100° F. (37.8° C.) or 101° F. (38.3° C.) for a few days. If a satisfactory pleural reaction is produced effusion will develop. Fifty-three patients in Brock's series were treated by pleurodesis; in three cases he used poudrage with talc by the method of Bethune,[6] but he found that silver nitrate was less disturbing and simpler to repeat after the initial thoracoscopy. Other substances, such as "gomenol" in olive oil, hypertonic glucose solutions, or blood, have been used by some workers. The principle of pleurodesis by chemical irritation in these cases seems well established, even though there is as yet no agreement about the most suitable agent for this purpose.

RADIATION SICKNESS

Some of the immediate effects of radiation on the human organism are inhibition of enzyme action, death of dividing cells, changes in cell permeability, and reduced flow of saliva. To the patient the most unpleasant feature of radiotherapy is often the sickness which may make life miserable and interfere with treatment. The symptoms are nausea, with or without vomiting, and lassitude. The vomiting reflex is set in motion by abnormal stimuli to the afferent nerve endings, abnormal sensitivity of the reflex pathway at some point, or abnormal irritability of the muscles which are involved in vomiting. With nausea the same abnormalities are presumably present but below the necessary threshold to produce vomiting. Psychic factors have been suggested as the cause, but, while they may have an influence, no one with experience can consider that sickness due to the effects of radiation is not a real entity. The somatic changes must be chemical or nervous. There is no evidence, however, of a direct effect of radiation on the conduction of a nervous impulse. The possibility of inhaled toxic gases can be excluded with modern apparatus; and, since the vomiting frequently occurs when no radiation is given to the stomach or to any part of the reflex arc involved in vomiting, it seems likely that endogenous chemical changes are responsible. Whether the chemical abnormalities in the blood reaching non-irradiated parts of the body are due to irradiation of the serum, changes in cell permeability, actual breakdown of cells, or to the effects of irradiation on endocrine function is not known. The last is not a likely primary effect, since sickness can occur after irradiation of any part except the limbs, but it is possible that the chemical changes brought about by radiation might cause some hormonal disturbance.

The cause can probably be found in changes in the metabolism of cells which are sensitive to radiation. Sickness occurs most frequently after high doses to parts of the body which are very vascular, such as the neck, thorax, and abdomen. It has been noticed that quite small doses produce sickness in patients with lymphatic leukaemia and, to a less extent, myelogenous leukaemia; this suggests that the breakdown of blood cells, probably lymphocytes, may set free substances in the circulation which produce the vomiting. It is commonly held that histamine-like substances are primarily responsible for *x*-ray sickness, since tissue damage brings about their release. Indeed, histaminase has been used with moderate success as a remedy,[1] and "benadryl" has been reported as efficacious.[2] Kullander,[3] however, holds a contrary view. He found that the vomit of patients with radiation sickness is usually hypo- or achlorhydric, though test meals showed normal gastric hydrochloric acid after the sickness had passed off. He also found that the administration of 20–40 minims (1.2–2.4 ml.) of 7% hydrochloric acid in water before meals and after *x*-ray treatment gave prompt relief. On the assumption that histamine would increase the secretion of hydrochloric acid he injected 0.125 mg. of histamine before meals; this also relieved the symptoms. If the effects of radiation were due to histamine-like substances, presumably the symptoms would have been aggravated by the injections. Brick[4] has recently shown that large doses of radiation to the stomach (2,500–6,000 r) may cause damage leading to ulceration and perforation, necessitating partial gastrectomy in some cases. This complication did not develop until 2–3 months after the radiation, and it was not associated with any lowering of gastric acidity. *X* rays have been advocated by some authors for depressing gastric acidity during the treatment of peptic ulcer. Brick's work has demonstrated the danger of this procedure, and in any case, as Kullander has shown, acidity very quickly returns to normal after radiation. Any estimate of the value of remedies for radiation sickness must take account of the influence of secondary effects due to sepsis, loss of taste, interference with nutrition, and intestinal hyperactivity.

It has been claimed that many other remedies besides those already mentioned have given good results. Among these are sodium chloride, magnesium chloride, high carbohydrate diet, large amounts of fluid, vitamin C, vitamin B, and amphetamine. They have all had relatively short periods of popularity. A recent report[5] on the value of pancreatin again suggests that the mechanism of digestion is disturbed. Pyridoxin, given by mouth or intravenously, is at present the most popular and successful drug used

[1] Ellis, F., *Brit. J. Radiol.*, 1942, **15**, 174 and 194.
[2] Lofstrom, J. E., and Nurnberger, C. E., *Amer. J. Roentgenol.*, 1946, **56**, 211.
[3] *Acta radiol., Stockh.*, 1947, **28**, 221.
[4] *New Engl. J. Med.*, 1947, **237**, 48.
[5] Quimby, W. A., *W. Va med. J.*, 1947, **43**, 80.
[6] *Radiology*, 1943, **41**, 383.
[7] Shorvon, L. M., *Brit. J. Radiol.*, 1946, **19**, 369.
[8] Van Haltern, H. L., *Radiology*, 1946, **47**, 377.

for radiation sickness in this country. Maxfield[6] and his colleagues in the U.S.A. first used it for this purpose, and its value was confirmed later by others.[7 8] It counteracts the reduction in the white cells caused by radiation—vitamin C appears to have a similar action. Exactly how pyridoxin relieves radiation sickness is a mystery the solution of which may be of great biological importance. If hydrochloric acid can produce the same good results, however, its cheapness and ease of administration should be in its favour.

NYSTAGMUS IN PELLAGRA

Doctors who underwent the grim ordeal of caring for their fellow prisoners in Japanese prison camps were able to collect much interesting information on the effects of chronic malnutrition. Disabilities were observed which had not hitherto been recognized as due to dietary deficiency; these included retrobulbar neuritis and the painful condition described as "electric" feet. There has also been some evidence that malnutrition caused a number of other strangely assorted symptoms, including such oddities as troublesome nocturnal diuresis and the appearance of violet hallucinations when the prisoners attempted to read.

Some observations by Raadt[1] on prisoners of war in camps at Bandoeng, Batavia, and Pakan Barol suggest that a group of oto-neurological disturbances, presumably associated with the early stages of pellagra, should now be added to the other signs of malnutrition seen in these tropical camps. The symptom complex included vertigo, tinnitus, subjective deafness, headaches, nystagmus, and weakness of lateral gaze and convergence, but not all affected prisoners had all these symptoms. Apparently the most noticeable objective symptom was the nystagmus, which occurred in typical cases as a rhythmical to-and-fro movement of the eyeballs in a horizontal direction. In some prisoners the nystagmus was constant, but in others there were intermittent attacks which were often precipitated by attempts to look sideways or by changes in the position of the head. Such attacks were usually accompanied by vertigo and sometimes by vomiting. The vestibular system was tested by pouring ice-cold water into the ears of prisoners with latent nystagmus or with active nystagmus which was checked by directing the eyes on a point beyond the range of oscillation. This procedure induced temporary nystagmus in normal subjects, but the irritability of the prisoners was abnormally high and the test often caused vertigo, sweating, vomiting, headaches, and even diarrhoea and fainting. Further tests in which the subject was turned round on a stool led to such unpleasant consequences that the prisoners became unwilling to co-operate. Less disturbing, however, were walking and pointing tests, and these often revealed abnormalities.

It might at first sight appear that the nystagmus was due to a peripheral nerve lesion, but the fact that some prisoners had nystagmus without defective hearing was taken as evidence against this view. A disturbance in the central nervous system, presumably involving the vasomotor reactions of the brain stem, seemed a more probable explanation of the symptoms. Raadt was unable to examine the composition of the diet or to test the curative action of nutrients suspected of being deficient, but he points out that vertigo is well recognized as a frequent and early feature of pellagra, while American workers[2 3] have also mentioned nystagmus as an occasional symptom. It seems probable that the early stages of pellagra are often overlooked or mistaken for neurasthenia. In the fully developed disease the attention of the clinician is so occupied in treating the familiar dermatitis, diarrhoea, and delirium that vestibular abnormalities would be of minor interest even if the patient was in a fit state to be examined. It is perhaps understandable, therefore, that early oto-neurological abnormalities should hitherto have attracted little attention.

1 *Acta oto-laryng., Stockh.*, 1947, **35**, 231.
2 Kinnear Wilson, S. A., *Neurology*, 1940, London.
3 Lewy, F. H., Spies, T. D., and Aring, C. D., *Amer. J. med. Sci.*, 1940, **199**, 840.

PULMONARY ARTERIOVENOUS FISTULA

Pulmonary arteriovenous fistula, in which there is a shunt of blood from pulmonary arteries to veins, is a congenital condition which has been recognized during life only a few times. In a recent paper Barnes[1] and his co-workers mention that they have found reports of 23 cases and they add two of their own, but wider knowledge of the existence of the condition may show it to be much more common than this figure suggests. The conspicuous outward signs are cyanosis, polycythaemia, and finger clubbing, with the result that congenital heart disease or polycythaemia rubra vera might be mistakenly diagnosed. The ascertainment of a pulmonary arteriovenous fistula is not merely of academic interest but practically important, since pneumonectomy can restore the patient to normal health. Burchell and Claggett[2] have described a successfully treated case and reviewed eight others recognized clinically, four of which were also cured by surgical excision.

An analysis of these reports shows a stereotyped syndrome, with dyspnoea, dizziness, and haemoptysis as the commonest symptoms and cyanosis, clubbing, and polycythaemia the typical signs. The heart is usually not enlarged, but on radioscopic examination one or more nodular pulsating shadows will be seen in the lung field, with increased hilar pulsation on the side of the lesion. Most of the patients have had small capillary haemangiomas of the skin or mucous membranes, and these should provide a valuable clue to the existence of the pulmonary lesion. A murmur either systolic or continuous as in patent ductus arteriosus is sometimes heard on the chest wall. The red cell count is 6 to 9 million, with a haematocrit finding of 60 to 80% erythrocytes and an increase in blood volume. The arterial haemoglobin–oxygen saturation in the four cases in which this was determined was the same in all—namely, about 70%.

Such unvarying results are regarded by Burchell and Claggett not as a chance occurrence but rather suggesting a compensatory mechanism which by an increase of cardiac output holds the arterial oxygen tension at a certain necessary level. However, they do not report any estimation of cardiac output in their patient, and, as Taussig and Blalock[3] have pointed out, very low arterial oxygen saturation shows the absence of any such mechanism in the tetralogy of Fallot. After pneumonectomy the polycythaemia quickly disappeared in Burchell and Claggett's case and in the case successfully treated by Barnes and his colleagues. In the latter the red cells numbered 9.5 million per c.mm. before operation; a week after operation the figure had fallen to 6.4 million, and ten days later it was 5.4 million. There should be no difficulty in correctly diagnosing this condition if it is borne in mind when the conspicuous symptoms are those which at first sight suggest congenital heart disease, polycythaemia rubra vera, or chronic lung lesions accompanied by cyanosis.

1 *Thorax*, 1948, **3**, 148.
2 *Amer. Heart J.*, 1947, **34**, 151.
3 Ibid., 1947, **33**, 413.

THE ORIGINS OF CARDIAC PAIN

Fifty years ago Huchard[1] drew up a list of eighty theories which might account for cardiac pain; facts have since disproved most of them. It is now the general opinion that both cardiac effort pain and the pain of myocardial infarction are the result of myocardial ischaemia. There is extensive evidence, conveniently summarized by Fishberg,[2] to support this theory. Thus, induced anoxaemia tends to provoke anginal pain; and the transitory changes in the electrocardiograph are of the same type in coronary thrombosis, coronary arteriosclerosis, experimental coronary obstruction, and induced anoxaemia. Sutton and Lueth[3] concluded from animal experiments that the pain of coronary occlusion was due to myocardial ischaemia, though there is also a possibility that pain can arise from direct stimulation of the nerve plexus surrounding the coronary arteries.[4] Further support is given to the anoxaemic theory by the well-known fact that obstruction of the blood supply to skeletal muscle during exercise produces severe pain, relieved by rest or removal of the obstruction.

Recently there have been suggestions that cardiac pain can have other origins. Hirsch and Orme[5] take anatomical facts into consideration, and Wyburn-Mason[6] in this *Journal* argued mainly on clinical grounds. The former suggest that cardiac pain arises in and about the coronary arteries rather than in the muscle tissues in the same way as pain occurs with sudden thrombosis of a peripheral artery. They draw attention to the many myelinated nerve fibres which are distributed in the fibrous tissues along the coronary arteries and which terminate in the walls of these arteries. They believe these nerves are sensory, and they refer to a similar pattern of sensory innervation which has frequently been described in peripheral systemic vessels. To support their theory they mention the conclusion of Katz and his colleagues[4] that in experimentally induced coronary artery pain the sensory response was due not to occlusion of the coronary artery but to direct stimulation of afferent fibres around the coronary vessels. These anatomical observations can hardly be used as evidence against the theory that cardiac pain is due to anoxaemia; at the most they indicate other possible mechanisms. All non-muscular tissues of the heart have a rich sensory innervation,[7] and in animal experiments cardiac pain appears to arise both from direct stimulation of coronary nerve plexuses and from local anoxaemia. It seems reasonable to suppose that in man the nerve plexuses can act either as a path for pain or as a starting-point.

In putting forward what he called "a new conception" of angina pectoris Wyburn-Mason described a number of cases in which anginal pain occurred without any abnormality of the heart. He added a list of conditions in which angina and vasodilatation, local or general, are said to coincide, and, interpreting this coincidence as a causal relationship, he suggested that the common factor which gives rise to anginal pain in coronary artery disease and in disease of neighbouring tissues is vasodilatation. Unlike Hirsch and Orme, he considered that the fibres which conduct the protopathic pain impulses are the unmyelinated vasodilator fibres which run by way of D1–5 posterior nerve roots, fibres which supply the mediastinal tissues including the heart. Any excess of vasodilator impulses in these nerves might lead to abnormal nervous activity and therefore pain impulses. Discussing angina of cardiac origin, Wyburn-Mason suggested that during increased cardiac activity the afferent nerve endings are stimulated by metabolites which collect because coronary sclerosis prevents vasodilatation. The presence of these metabolites causes abnormal reflex impulses in the coronary vasodilator pain fibres, and the immoderate attempt at vasodilatation gives rise to pain.

Although the concept of frustrated vasodilatation being painful in this manner is a novel one there seems little else to recommend it. To the same category belongs the theory that although accumulated metabolites stimulate the nerve endings of pain yet they cause pain only through the excess of reflex antidromic impulses. Many problems connected with angina remain unsolved; no doubt it may develop in the absence of cardiac disease or be absent in the presence of gross myocardial ischaemia, but it still does not seem possible to approach nearer to the truth of the matter than Fishberg's summing up, that angina pectoris is the cry of the heart for more oxygen.

[1] *Traité Clinique des Maladies du Cœur et de l'Aorte*, 1899, **2**, 77. Paris.
[2] *Heart Failure*, 1940, London.
[3] *Arch. intern Med.*, 1930, **45**, 827.
[4] Katz, L. N., Mayne, W., and Weinstein, W., ibid., 1935, **55**, 760.
[5] *Arch. Path.*, 1947, **44**, 325.
[6] *British Medical Journal*, 1948, **1**, 972.
[7] Woollard, H. H., *J. Anat., Lond.*, 1926, **160**, 345, and *Heart*, 1926, **13**, 319.

THE NATURE OF SEBUM

It is about 300 years since Malpighi first described the sebaceous glands. Boerhaave added to this description, but it was not until the latter half of the nineteenth century that much interest was taken in their function. In our own time some authorities have suggested that nervous and endocrine factors influence the secretion of sebum, but few quantitative observations have been made. Schur and Goldfarb[1] in 1927 estimated the quantity of sebum secreted on the forehead by wiping with small cotton wads the area of skin to be tested. They found that the layer of sebum on the surface of the skin reappeared very rapidly, often within 15 minutes of its removal, but did not exceed the original amount even after an interval of two hours. They therefore concluded that the amount of sebum over a given area of skin was constant and that secretion stopped when a certain level was reached and started again when the amount fell below that level. Emanuel[2] confirmed this observation and found that isolation of the area for one week produced no increase in the thickness of the layer. This was not constant but varied from day to day within a range characteristic for a given area. He concluded that the thickness was regulated by an interaction between two opposing factors: the resistance of the sebaceous layer and the functional capacity of the glands. The former was proportional to the thickness of the layer and the consistency of the sebum and the latter depended upon the size of the glands. The rate of reproduction of the layer appeared to be dependent upon the number of glands in the area in question. Dunner[3] also concluded that the sebum level was dependent on the viscosity of the sebum. He showed that a rise in external temperature raised the productive capacity of the glands and the thickness of the sebum layer.

Recently Butcher and Parnell[4] have made some interesting observations on the quantity and composition of sebum secreted on the heads of three individuals of different type. In one man with a dry scalp and dandruff there was an average of 0.168 mg. of fat and 0.0171 mg. of cholesterol per sq. cm. when specimens were taken once a week over an eight-week period, the cholesterol being 9.4% of the total sebum. In another man with an oily scalp and sparse hair there was an average of 0.219 mg. of fat and 0.0149 mg. of cholesterol per sq. cm. over the same period, 6.3% of the total sebum being cholesterol. In the third man, with good hair and little dandruff, there was an

[1] Schur, H., and Goldfarb, L., *Wien. klin. Wschr.*, 1927, **40**, 1255.
[2] *Acta derm.-venereol., Stockh.*, 1938, **19**, 1.
[3] *Dermatologica, Basel*, 1946, **93**, 249.
[4] *J. invest. Derm.*, 1947, **9**, 67.
[5] *The Hair and Scalp*, 1944, London.

average of 0.160 mg. of fat and 0.0119 mg. of cholesterol per sq. cm., the cholesterol being 7% of the total sebum. When collected daily there was only slightly less sebum for a given period than when collected weekly, and frequent removal of the sebum did not cause increased oiliness of the scalp.

In the past there has been some doubt whether sebum contains cholesterol, though Savill[5] mentions it as being present. In Butcher and Parnell's cases the highest content of cholesterol occurred in the individual with the greatest desquamation of the scalp. Had the cholesterol originated in the desquamating cells, then the collection made weekly should have contained the greatest proportion of cholesterol, but this was not the case. Butcher and Parnell also investigated the effects of resistance on the secretion of sebaceous glands. They found in the rat that when the skin was covered, or a resistance created, the gland did not become smaller but enlarged from accumulation of cells and sebum within it. This accumulation is similar to that present in sebaceous cysts.

THE COURSE OF RHEUMATOID ARTHRITIS

In few diseases is it more difficult to form an unbiased opinion about the value of different methods of treatment than in rheumatoid arthritis. Its onset may be acute or gradual, and remissions or exacerbations occur for no obvious reason; remedies which have proved helpful in one case are perhaps ineffective or even harmful in another. In some cases the condition becomes quiescent for months or years and then relapses, while in a proportion variously estimated at 50% to 70% the disease is permanently arrested, though often severe crippling deformities remain. Two hundred and fifty patients who received only simple medical or orthopaedic treatment for rheumatoid arthritis have been studied by Short and Bauer[1] at the Massachusetts General Hospital over a long period of years. They point out that in nearly all similar investigations the details given have been insufficient to make comparisons practicable. They have therefore evolved a system of observation and record which might be used as a standard. The course of the disease must be followed in many more cases before definite conclusions can be reached, and general practitioners could well undertake some of the necessary research, since they have their patients under constant observation and it would not make excessive demands on their time or require special training or equipment.

The results of Short and Bauer's observations confirmed certain general impressions. Their patients were admitted to hospital between 1930 and 1936; in all of them the usual physical signs of rheumatoid arthritis were present. They generally remained in hospital for three or four weeks for investigation and for instruction in simple remedial measures which could be carried out at home, including appropriate diet and physiotherapy. Thereafter they reported back to the hospital once or twice a year if practicable, or they were interviewed by trained observers and their condition noted. When necessary they were readmitted to hospital for special treatment. The average duration of observation was 9½ years, with a range from six months to 16 years. In slightly over 50% improvement took place, and complete recovery in 15%. Fifty-two patients were given fever therapy and 16 had blood transfusions, but in neither of these groups were results better than in the cases which had no special treatment. Of those who improved within two years 37% later relapsed, compared with 28% of recorded relapses in a combined series, taken from the literature, of 768 patients who originally improved with gold therapy.

[1] *New Engl. J. Med.*, 1948, **238**, 142.

Investigations of this type will always be complicated by the fact that in the course of rheumatoid arthritis outside influences may turn the scale one way or the other. The mere fact of being under regular observation has an encouraging effect, and the suggestion that therapeutic resources have been exhausted does much to weaken the patient's power to fight the disease: one American authority with wide experience has said that though he is doubtful if vaccines have any specific effect he uses them in small doses in order to keep the patient under continual observation and thus control the general line of treatment.

ARSENIC AS A CAUSE OF CANCER

Prolonged arsenical therapy can cause cancer of the skin and other organs, and there is a risk of occupational cancer among workers making arsenical compounds. Sir Jonathan Hutchinson in 1887 was the first to draw attention to the development of cancerous ulceration on keratoses following the use of arsenic in the treatment of psoriasis. Though arsenic was used widely to treat skin diseases, syphilis, and many other general diseases it would seem that in psoriasis there is some particular predisposition to this grave complication of treatment. Apart from the more obvious forms of cancerous ulceration, superficial scaling and keratotic lesions and multiple small intra-epidermal carcinomata of a benign type are often seen, more particularly on covered parts. The lesions may remain stationary, or involute, or they may progress to more malignant forms.

These changes may appear within a few years of the beginning of treatment or exposure, or they may be delayed up to 40 years. In a comprehensive review of the subject Neubauer[1] states that an average interval is 18 years. Arsenic is a normal constituent of body tissues, and small amounts may be found in skin, hair and nails, and urine; the quantities vary slightly with the geographical situation, the character of the drinking-water, and other factors. The finding of arsenic in the tissues, therefore, is not necessarily significant when the cause of a cancer is being considered. Neubauer states that the results of chemical investigation are disappointing; definite conclusions cannot be drawn either from the absence of arsenic from the tissues or from its presence in small amounts. Animal experiments have produced only doubtful results, and further knowledge of the pathogenesis of arsenical cancer may not be obtained until the pharmacology of arsenic is better understood. Barry, Bunbury, and Kennaway[2] have suggested that arsenic may induce cancer not by direct action but by causing accumulation in the tissues of organic (carcinogenic) compounds which would normally be oxidized or reduced to other forms. Occupational cancer of the skin and lungs has been reported in workers engaged in factories producing sheep dip and insecticides, and in rare instances cancer of the skin in gardeners and in metal-miners and smelters has been attributed to arsenic.

Sir Reginald Watson-Jones will deliver the Robert Jones Lecture on "The Reactions of Bone to Metal" before the Royal College of Surgeons of England (Lincoln's Inn Fields, London, W.C.) on Thursday, Dec. 9, at 5 p.m.

Dr. W. H. Wynn, F.R.C.P., will deliver the FitzPatrick Lectures on "The Pestilences of War" before the Royal College of Physicians of London (Pall Mall East, S.W.) on Tuesday and Thursday, Dec. 7 and 9, at 5 p.m. In the first lecture Dr. Wynn will speak on "The Early Civilizations and Greece," and in the second on "The Roman Republic and Empire."

[1] *Brit. J. Cancer*, 1947, **1**, 192. [2] *Biochem. J.*, 1928, **22**, 1109.

THE INSTITUTE OF OPHTHALMOLOGY

The Institute of Ophthalmology, one of the federated institutes of the British Postgraduate Medical Federation in the University of London, was opened formally on Nov. 4. The buildings of the Central Eye Hospital in Judd Street, King's Cross, have been largely reconstructed internally to serve the Institute. The Institute has grown out of the medical schools of the three amalgamated hospitals—the Central Eye Hospital itself, Moorfields, and Westminster. These schools have been in existence for many years, the one at Moorfields dating back as far as 1810.

The work to be carried out at the Institute will be twofold—postgraduate teaching and research, both in laboratory work and on clinical material. Teaching will be available to qualified students from all over the world who wish to train as specialists in ophthalmic medicine and surgery. It was stated that at the present time students from seven countries, not including the British Isles, are taking courses at the Institute. For the present term 126 students are enrolled. Three main research teams of the Medical Research Council are carrying on work there. They are an ophthalmological research unit working under Sir Stewart Duke-Elder on the physiology of the eye and ocular diseases, a vision research unit under Professor H. Hartridge, and an industrial illumination unit working under Mr. Weston on the practical aspects of lighting. In addition the Institute may be made available for individual research. There are also a pathological department, which carries out all the routine bacteriological and histological work of the hospital and conducts research in these fields, and a department of medical illustration, which includes a well-equipped photographic studio with dark-rooms, photomicrographic apparatus, and printing facilities. The ophthalmological library and museum are said to be the most complete of their kind in any country. Great skill has been shown in adapting the old hospital buildings to this new function.

The Earl of Rothes, chairman of the committee of management, who presided over the opening ceremony, referred to the help of the British Postgraduate Medical Federation in sponsoring this enterprise. Sir John Herbert Parsons spoke of the high reputation of the three hospitals as teaching schools, and said that in the new Institute this tradition would be enhanced because the teaching would be carried out under much more favourable circumstances. The large amount of research already done by the staffs of the hospitals would be continued on a wider basis. The Institute would be under the supervision of Sir Stewart Duke-Elder, and this fact alone would ensure its success.

Greetings from America

Professor Alan Woods, director of the Wilmer Institute, Johns Hopkins University School of Medicine, brought the congratulations of American ophthalmology, and said that the founding of such an Institute was the rational outcome of long and industrious work in ophthalmology in Great Britain. The independent or semi-independent hospitals in Europe and America had provided a good basis for present and future service, but a new type of institution was needed for research and the advancement of the frontiers of knowledge. Most of the obvious things had been done, and modern ophthalmic research must include the application of biophysics, bacteriology, and related sciences to the study of the normal and the abnormal eye. But advances along these lines could not be made unless the scientists undertaking the work were specially trained, and the help of biochemists, biophysicists, and others was needed. In short, new types of investigators were required.

The type of institute now being dedicated afforded the answer to this quest. Ophthalmological research must be a university undertaking, so that the investigation could be co-ordinated, access made possible to clinical material, and fellowship offered with colleagues in other branches of medicine. In a university school of medicine an ophthalmological institute must be regarded as an integral unit. It was typical of British courage to undertake this task in the midst of so much other reconstruction. Anything which his own school of medicine could do to assist would be only a small acknowledgment of the debt it owed to British ophthalmology. He extended to the new enterprise good wishes for success and high achievement.

Greetings were also given by Professor H. J. M. Weve, of Utrecht, who said that this was a great day not only for ophthalmology in London but throughout the world. Ophthalmology could not be looked upon as a science apart from the rest of medicine; all parts were interlocked, and the fact that the Institute was part of the University of London showed that that was recognized in this country. England had contributed much to the study of this specialty through many of its distinguished workers, notable among whom was Sir John Parsons.

It was stated that the amalgamated hospital is the largest specialist eye hospital in the world and the Institute the first of its kind in Europe. The practice of the hospital, drawing as it does patients from the entire London area and indeed from all over the United Kingdom, provides material for teaching and research which is unrivalled in any country.

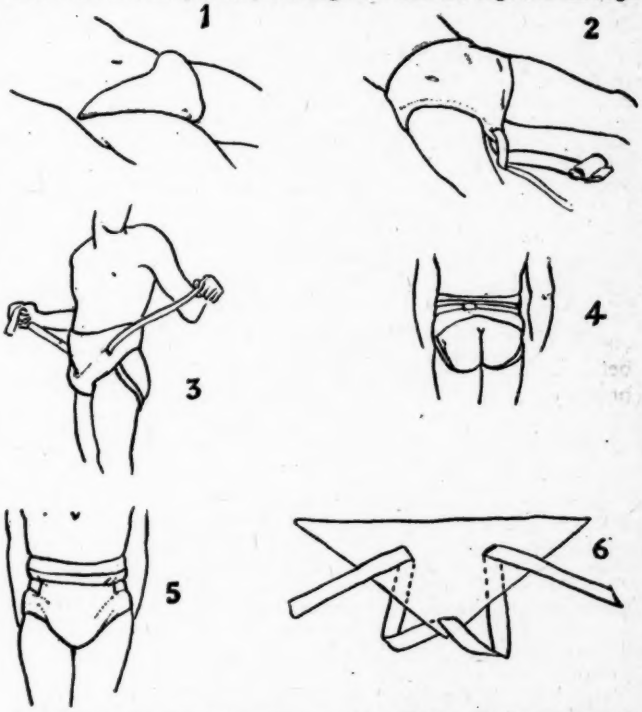
Later in the day Professor Alan Woods delivered the inaugural lecture on experimental studies on the pathogenesis and therapy of ocular tuberculosis.

Preparations and Appliances

A SCROTAL BANDAGE

Mr. B. JOHN MAXWELL, a student at the Liverpool University Medical School, writes: Several excellent methods of bandaging the scrotum are already in everyday use. Prominent among them are the roll bandage, the T bandage, and the Belleview adhesive plaster methods.

The roll bandage method is simply the winding of a figure-of-8 with a 4-in. (10-cm.) bandage so that the legs are through



1.—Wool pad shown in position with rolled apex supporting the scrotum. 2.—Roll bandage threaded through apical hole. 3.—Roll bandage brought to and threaded through the basal holes. 4.—Bandaging completed; showing bandage following fold of buttock upward and forward. 5.—Complete. 6.—Showing position of holes and direction of bandage.

the loops: the loops are held up to waist level by alternate complete turns round the abdomen. In applying a T bandage, the joint should be at the back, the stem of the T coming between the legs from the back and up to the front to give support to the scrotum. In the Belleview method a piece of "elastoplast" 36 in. by 4 in. (90 by 10 cm.) has two mid-width slits cut from each end, but not to meet at the centre: this gives an H-shaped piece, the bar of which is padded with gauze and applied to the scrotum in such a way that the two upper limbs of the H are passed either side of the penis

and applied to the abdominal wall and the two lower ones curve laterally following the folds of the buttock. The out-patient who requires daily scrotal dressings is, however, still a problem, as the roll bandage and the T bandage methods need great skill and take a certain amount of time if slipping, rolling, and rubbing are to be avoided, while the Belleview plaster is extremely painful to take down each day.

The method described below has the advantages that not only does it give comfort, support, and security, but it is easy to put on, taking little time, and it need not be removed for defaecation. All that is required is a triangular bandage, a 3-in. (7.5-cm.) bandage, cotton-wool, and some 1-in. (2.5-cm.) adhesive tape.

The patient lies on his back and the dressing is applied to the scrotum. A triangle of wool has its apex rolled up into a firm pad which is placed underneath the scrotum, acting as a support, and the rest of the triangle of wool covers the scrotum so that the base of the triangle reaches the peno-scrotal junction (Fig. 1).

The triangular bandage has a piece of 1-in. adhesive tape stuck on to it about 2 in. or 3 in. inside the apex and a slit cut into it (the plaster is only to reinforce the edges of the hole in the bandage). The triangular bandage is now placed over the wool, again base upwards, so that the apical hole lies in the crutch posterior to the wool pad. Two more pieces of adhesive plaster are stuck on to the triangular bandage 1 in. above and medial to the anterior superior iliac spines and slits cut into them (Figs. 3, 5, and 6).

The basal corners are now tied round the back and 2 ft. (60 cm.) or more (depending on the obesity of the patient) of the roll bandage is threaded through the apical hole (Fig. 2). The bandage is drawn back between the legs and laterally, following the folds of the buttock, upward and forward (Fig. 4), deep to the triangular bandage, to the basal holes, through which it is threaded (Fig. 3). The roll bandage is now taken across the back and wound round the body over the triangular bandage (Fig. 5). The end is strapped down with adhesive tape. To complete the bandage a hole is made through which the patient can micturate.

Important points are: (1) Before tightening the bandage by traction on the apex the scrotum should be drawn upwards. This, together with support from the wool pad, gives " lift " to the scrotum. (2) The basal holes should not be made until they have been tried for position. (3) The lines of pressure lie between the three holes; therefore it is essential that the wool should extend beyond the pressure-lines to prevent rubbing. (4) The patient should be allowed to decide where he wants the hole through which he will micturate.

The completed bandage is neat and comfortable and needs little skill in its reapplication.

I would like to thank Professor C. A. Wells for his advice and criticism, and for the services of his artist.

The Nurses and Midwives Whitley Council have agreed on new training allowances, which will take effect from Sept. 1, for student mental nurses employed in the National Health Service. They are regarded as the basis on which true student status can be built up, bringing mental-nurse training more closely into line with training in other professions. The responsibilities resting upon student mental nurses and the exacting nature of the work in mental institutions are recognized in the allowances payable to them. Men and women will receive the same training allowances. Additional dependants' allowances will be paid to help those with family responsibilities. For students recruited on or after Jan. 1, 1949, the first-, second-, and third-year allowances will be £230, £240, and £255 respectively. Students will also receive proficiency allowances of £20 and £30 respectively on completing the second and third years of training if they pass the appropriate examinations. Students who live in accommodation provided by the employing authority will pay £100 a year for board and lodging. For existing female and resident male students, or such students recruited before Jan. 1, 1949, the allowances, with effect from Sept. 1, 1948, are £130 in the first year, £140 in the second year, and £155 in the third year, the emoluments being valued at £100. These students will also continue to receive proficiency allowances. Uniform will continue to be provided and laundered without charge for all students. Non-resident students will also receive free meals on duty. Where in exceptional cases existing salaries are higher than the new allowances students will be entitled to retain them. These scales represent an increase of £30, £40, and £50 per annum respectively on the previous basic rates for female students. The additional annual cost to the National Health Service will be in the neighbourhood of £65,000. The settlement has been accepted by the nurses' representatives on the understanding that a special committee of the Council will be set up to consider the working conditions in mental hospitals and to recommend measures necessary to achieve full student-nurse status as soon as possible. The management side have agreed to take all measures in their power to put into force any recommendations on the matter adopted by the Council.

Correspondence

The Training of a Doctor

SIR,—The comments in this letter are inspired by Professor J. A. Ryle's letter (June 12, p. 1153). In this he rightly deplores the lack of attention given to psychosomatic medicine in the curriculum. Herein I believe lies the pointer to the future development of general practice as we understand the term. All thinking members of our profession must be depressed when we consider the future of the general practitioner. We are all conscious of the development of the type of practitioner who takes progressively less and less clinical responsibility, who spends his day prescribing medicine, and promptly refers all sick patients for either indoor or outdoor hospital supervision. I greatly fear that the general practitioner of the future is menaced by this degradation of his professional function into a signer of forms and a director of patients to an appropriate hospital department.

There is, however, a dignified and academically honourable alternative. I feel strongly that the general practitioner as we know him should develop into a sound psychosomatic physician. He must certainly retain his character of family physician. This tie will in fact be tightened rather than slackened as a result of his training in psychosomatic medicine. He will be equipped as few general practitioners are at present to explore that vague hinterland of medicine where the organic and the functional join hands to play such havoc with his patients. A more intimate knowledge of organic medicine will be necessary than that of the present general practitioner, perhaps a standard intermediate between that of the present practitioner and the standard required for membership of the Royal College of Physicians.

Such a standard is by no means beyond the capacity of the average medical graduate, since he will be relieved of the obligation of being in addition surgeon, gynaecologist, and obstetrician to his patients. These functions must be left in the hands of more capable performers than the average general practitioner. It has been well said that no operator should open an abdomen to remove a simple appendix unless he is prepared to remove a foot of bowel if necessary. The general practitioner must face up to the ultimate loss of surgery, gynaecology, and obstetrics. However, I see his status increased rather than diminished by the development outlined above.

This professional keystone to the arch of medical service must be vested with great authority and responsibility. With apologies for mixing my metaphors, he must be the captain of his patient's ship of health, deserting or sharing the bridge for brief interludes only while the surgical or other specialist pilot negotiates his own highly localized reefs and channels. From his ranks will be drawn the most able, to become the consulting and teaching physicians as we know them to-day, but with this difference: that they will have graduated from the ranks of psychosomatic family physicians rather than from the medical registrars of teaching hospitals, a consummation devoutly to be desired.

It may be objected that there will always be a need for the all-rounder type of doctor in the outlying country areas. This will be true only to a very limited extent. I feel sure that, with the aerialization of transport, surgery, gynaecology, and obstetrics will increasingly be relegated to institutions even for country patients.

To summarize, I feel that the present trend in medical practice is on the one hand the production of specialists with a much too academic background, and on the other hand the professional degradation of the general practitioner to a glorified medical clerk. This general trend is most deplorable, and I suggest the development outlined as a logical and dignified alternative.—I am, etc.,

Sydney, Australia. LANCE HEWITT.

Surgical Treatment of Ménière's Disease

SIR,—In an annotation on the surgical treatment of Ménière's disease (Nov. 6, p. 829) you kindly referred to the operation I employ for the relief of vertigo in suitable cases, saying, "This cures the vertigo without affecting the hearing." I have always found[1 2] that this operation, which consists in removing all or part of the membranous external semicircular canal, is followed

by total and irreversible loss of cochlear as well as vestibular function on the operated side.

For this reason it is reserved for cases in which the disease appears to be unilateral and the hearing on the affected side is seriously impaired and, as a rule, distorted. Such distortion is a characteristic and common feature of the deafness in Ménière's disease; it is particularly noticeable for musical and high-pitched sounds, and when present adds to the distress of the disease.

I have found that the loss of a distorted remnant of hearing in one ear, far from diminishing the general capacity for hearing, often leads a patient after an operation to say that his hearing is better because once again he can enjoy listening to music, and loud sounds no longer distress him. Thus whilst it is often true to say that the hearing capacity of patients subjected to my operation is altered, sometimes for the better, I would like to make it quite clear that the hearing in the operated ear is always lost, though for reasons already given such a loss often proves to be a gain.—I am, etc.,

London, W.1. TERENCE CAWTHORNE.

REFERENCES

1 *J. Laryng.*, 1943, **58**, 363.
2 *Ann. Otol. etc., St. Louis*, 1947, **56**, 18.

SIR,—In the annotation (Nov. 6, p. 829) on surgical treatment of Ménière's disease you state that Cawthorne's operation cures the vertigo without affecting the hearing. In one or two cases Day has succeeded in coagulating the labyrinth with retention of some of the hearing, but destruction of the labyrinth by any other method devised up to the present has involved destruction of the cochlea also.

The object of the operations devised to deal with the labyrinth itself was to avoid an intracranial operation, but the neurosurgeons, until Ray's recent paper, had claimed that the destruction of the vestibular portion only of the eighth nerve left satisfactory hearing. It is now generally recognized that the hearing remaining after Dandy's operation on the vestibular nerve is not satisfactory in most cases, and the risks involved are not merited by the results achieved.—I am, etc.,

Lincoln. M. SPENCER HARRISON.

SIR,—The paper on Ménière's syndrome by Mr. E. R. Garnett Passe and Dr. J. S. Seymour (Nov. 6, p. 812) prompts me to raise two points. The first relates to the case Ménière described in 1861. "It would seem," the authors state, "that acute haemorrhagic labyrinthitis was the cause of the syndrome." So far so good—but it is in my view essential to add that in the original and fatal case Ménière's syndrome has to be interpreted as a haemorrhagic symptom of acute leukaemia.

This leads to my second point. The organ of hearing (inner ear) and the organ of equilibrium (labyrinth) live in a semi-detached dwelling. These and their two cranial nerves (the cochlear and the labyrinthine nerve) are affected by a great variety of causes with the common feature that all can produce Ménière's syndrome. The outlook in Ménière's disease accordingly varies from death within a few days to complete recovery.

The term "Ménière's disease" is at present one of the vaguest in medical terminology, and to replace it by "Ménière's syndrome" has not helped to reduce the muddle. I believe that we should either discard the term altogether or agree that we mean something entirely different by it than Ménière meant to describe—namely, a haemorrhagic labyrinthine symptom.

Before recommending sweeping therapeutic measures we must try to group these greatly differing cases according to their proved or probable aetiologies, and in this respect we are still very much at the beginning. "Ménière," so Passe and Seymour complain, "had inadequate knowledge of the underlying aetiology." Alas, so have we. Surgical suggestions for the relief of symptoms of varying and obscure aetiology often seem initially successful. In the case of Ménière's disease they have included many different procedures, among them operations on the antra. So far they have all had one thing in common: they have not come to stay.—I am, etc.,

London, W.1. A. B. ALEXANDER.

Intussusception Due to Carcinoma of Colon

SIR,—Intussusception of the gut at either extreme of life is a fascinating lesion, and Mr. R. A. C. Owen's account of two cases of colonic intussusception due to a carcinoma (Oct. 30, p. 786) will be of interest to all surgeons. He raises three points of some academic importance with which I am not in entire agreement. In the first place I do not think that the condition is so rare as the published figures would indicate. In a limited surgical experience I have come across three cases of this type, and I think that most surgeons meet with at least one or two examples during their career. Moreover, it is not uncommon to find that a growth felt on rectal examination in the out-patient department proves to be in the lower pelvic colon when seen at operation; these are undoubtedly examples of recurrent intussusception of minor degree.

Then Mr. Owen suggests that colonic intussusception in adults is not necessarily associated with a carcinoma, but surely any other cause must be a rarity. In dealing with a colonic intussusception one looks for and expects to find a carcinoma, or at any rate a growth of some kind. I agree that occasionally a tumour is absent, and in one of my patients, who was a British soldier serving in India, no abnormality was found in the transverse colon, which had intussuscepted and was subsequently resected. Possibly his intussusception was due to the uncommonly active gastro-colic reflex from which most newcomers to the Tropics suffer and akin to the spate of intussusceptions which are said to afflict those of Mohammedan faith during the fasting season.

Finally, it is not strictly accurate to say that this condition is of necessity associated with a long and mobile pelvic colon. The essential feature is a mobile colon, and whilst the fulfilment of this requirement is usually confined to the transverse and pelvic portions of the large bowel it occasionally happens that the ascending colon also has a mesentery owing to faulty fixation of the gut to the abdominal wall during development; in the presence of an exciting factor this may result in an ileo-caecal intussusception. In a remarkable case at present in Mr. W. J. Ferguson's wards at the West Middlesex County Hospital a woman of 75 was subjected to laparotomy on account of symptoms of acute upon chronic intestinal obstruction. An intussusception of the colon was found lying below the spleen. It reduced with ease and proved to be of the ileo-caecal type. The whole colon from caecum to rectum was attached to the abdominal wall by a long mesentery, making a hemicolectomy a matter of extreme ease. The exciting factor producing the intussusception was a small papillary carcinoma encircling the ileo-caecal valve.—I am, etc.,

Isleworth, Middlesex. LOUIS A. IVES.

SIR,—Mr. R. A. C. Owen in his paper on the subject of intussusception in adults due to carcinoma of the colon (Oct. 30, p. 786) states that only two such cases have been reported in the literature in the last ten years. The following case would therefore seem worth recording.

A woman aged 74 was admitted to hospital in the evening of June 6, 1948, complaining that something had "come down" when she was straining at stool that afternoon. Her previous history was that after being constipated all her life she had had diarrhoea with three or four motions every twenty-four hours for two months before admission. No blood or slime was noticed in the stools. She had had a ruptured perineum in childbirth forty years ago. On examination she was a thin old lady. Examination of her abdomen was negative. A large intussusception was projecting five to six inches from the anus, with an annular papilliferous carcinoma at its apex. The intussusception was reduced to within the rectum, with the patient in the left lateral position, without an anaesthetic. The buttocks were strapped together and the patient was placed on her face with the foot of the bed raised to complete the reduction. On June 21 a laparotomy was performed through a right lower paramedian incision under a general anaesthetic. The growth was found to be in the sigmoid colon, and as there was no evidence of secondary deposits the sigmoid colon was resected with end-to-end anastomosis. After operation she did well and was discharged from hospital on July 19. When last seen, on Oct. 17, she was very well, with no symptoms at all.

The pathological report on the specimen was as follows: "The specimen consists of large bowel, 20 cm. in length. In the centre is a flattened papilliferous growth, 7 cm. in diameter, which com-

pletely encircles the bowel wall; it appears to be confined to the mucosal coat. Microscopic structure: the tumour is a well-differentiated adenocarcinoma."

My thanks are due to Mr. Donald Barlow, who performed the operation and has given permission for me to report the case.—I am, etc.,

Luton. H. BERNARD JUBY.

Purpura Fulminans Complicating Scarlet Fever

SIR,—I have read with great interest the article by Drs. T. Anderson, M. S. Ferguson, and J. B. Landsman in the *Journal* of Sept. 18 (p. 549) entitled "Purpura Fulminans Complicating Scarlet Fever." This work poses clearly the problem of pathogenesis of the haemorrhagic forms at the onset and of the haemorrhagic complications, either generalized or localized, in infectious diseases.

It is difficult to explain the aetiology of these haemorrhagic complications. It cannot be explained on the grounds of special virulence of the organisms, because in time of epidemics only a small number of patients are affected by these grave forms. The same can be said of the organisms responsible for reinfection or cross-infection so frequent in hospital environment and which very fortunately give rise to haemorrhagic manifestations only occasionally. We have therefore to admit that the affected subject responds in some peculiar way to the causative organism.

It has been frequently said that these haemorrhagic manifestations are of allergic nature. This interpretation is very unlikely, whether it be concerned with allergy towards the responsible organism of the primary disease or with hetero-allergy—viz., para-allergy as defined by Moro and Keller—to a different organism. Allergic manifestations usually do not show these dramatic features of the haemorrhagic complications in specific fevers, they do not cause such intense vascular lesions, they are in general not so serious, and, lastly, tests for allergy to the organisms incriminated have been uniformly negative.

It is my belief that the haemorrhagic syndrome observed by Drs. Anderson, Ferguson, and Landsman can be compared to the Sanarelli-Shwartzman phenomenon. A given infection can give rise in certain individuals to a transitory alteration of bodily response (*altération réactionnelle transitoire*) analogous to the response in the rabbit which has received a preparatory injection of a filtrate of organisms in the experiments of Sanarelli and Shwartzman. If at that precise moment the precipitating factor comes into play (this being either a persistent primary infection or a cross-infection or even chemotherapy) the result may be a haemorrhagic manifestation, either generalized or localized, unrelated to the intensity, gravity, or nature of the precipitating factor.

The haemorrhagic phenomenon has, indeed, nothing specific in itself and can be produced by various agents, a fact which is responsible for the belief that the real cause is sometimes chemotherapy, in others the persistence of an infection or septic focus, or in others a cross-infection. Moreover, two facts in the case of Dr. Anderson and his co-workers are of special interest: (1) Marked hypothermia—Sanarelli has produced experimentally in the animal a syndrome with hypothermia and haemorrhagic signs. (2) The spectacular action of penicillin can be compared to the specific immunization which neutralizes the toxin from the filtrate of bacilli, as shown in the Shwartzman phenomenon; the toxin having been rapidly neutralized, haemorrhagic manifestations do not occur.

In a series of papers, partly yet unpublished, I have shown the importance of the Sanarelli-Shwartzman phenomenon in human pathology with special reference to infection and chemotherapy. I have included all these facts under the general denomination of "sanergy" ("*sanergie*") and I believe that this new interpretation of a great number of facts of, until now, obscure significance will lead to search for rational treatment.—I am, etc.,

Hôpital Rothschild, Paris. S. LEWI.

Bornholm Disease

SIR,—On Oct. 4 a little girl aged 16 months was brought to me. She groaned with each expiration; inspiration was short and shallow; she looked anxious; the temperature was 100° F. (37.8° C.); the upper abdomen was rigid; and I could find no abnormal signs in the chest. Her mother reported she had been quite well the previous day and until suddenly attacked with pain at 5 p.m. on that day, but that she had had a similar attack on Oct. 2 from 11 a.m. till 6 p.m.

This child was sent to hospital as a matter of interest, with a tentative diagnosis of Bornholm disease. In hospital she was, to my mind unfortunately, given "sulphamezathine" and penicillin for a supposed pneumonia, the *x*-ray report stating there was a "slight increase in opacity in the right mid-zone." She returned home on Nov. 6 quite well and with no clinical signs of pulmonary disease.

In another village, three miles from the home of the child referred to above, a small boy aged 2 years was seized with a similar pain at 6 a.m. on Nov. 3; this continued, though lessening, till 6 a.m. on Nov. 4, after which he was well till 5 p.m. the next day, when the pain returned and continued till the late evening. He then slept well, and, apart from some guarding of his upper abdominal muscles which wore off in 24 hours, he remained well.

A child aged 4 years in the same village, who had been in contact with the small boy on Nov. 1, commenced with pain at 4 p.m. on Nov. 4 and it continued through the night, but she was well on the two following days. The pain recurred on Nov. 7 at 9 a.m., but eased by 12 noon; since then she has been well.

When first seen these patients all showed obvious pain and anxiety, short and suddenly checked inspiration, longer expiration (not an expiratory grunt), rigid upper abdomen, slight fever, and a preference to sit up rather than lie down. Onset had been sudden, with a definite time stated by the respective parents. Remission of symptoms was more gradual and followed as suddenly as before by a further attack.

All three were, to my mind, cases of Bornholm disease, which I think may possibly be more common than is generally suspected, and they illustrate the advisability of refraining from the blunderbuss use of "sulpha" drugs in cases of apparent respiratory disorder, if only that more precise diagnosis may be made possible.—I am, etc.,

Richmond, Yorks. A. F. T. ORD.

Fibrositis

SIR,—Before finally parting with a disease I thought I had suffered from for forty years may I put one question to those who have decided to abolish it? If, as they assert, all such troubles are due to articular lesions, how comes it that the distressing pains radiating from the supposedly fibrotic nodules can be so definitely relieved by massage of them, as I know from grateful experience that they can?—I am, etc.,

Elsted, Sussex. ERNEST JONES.

Vegetable Marrow Poisoning

SIR,—The following case of poisoning by a vegetable marrow may be of interest to some of your readers.

A retired professional gardener planted a seed in the soil of his allotment and in due time three normal-looking marrows were produced. The ground was clean and had not been manured previously, nor had any manure been used while the plant was growing. The first marrow was prepared in the normal way and served with meat and potatoes, but the taste was so bitter that the man and his wife and daughter spat out their mouthfuls and discarded their helpings without swallowing either marrow or juice. The second marrow was quite normal in taste.

The third was prepared some time later and served with mincemeat, beans, and potatoes. The daughter and husband noticed that this was again bitter and discarded their helpings without swallowing marrow or juice, but the wife, although discarding her helping of marrow, mixed the juice with the beans and potatoes and finished the meal. About five hours later she had a sudden attack of colicky abdominal pain, followed by intense vomiting and diarrhoea. She was prostrated, and her symptoms lasted through the night. The attack then decreased in severity till the following evening, when she was well enough to get up. She has been well since then.

The man sought advice from the local health authority, and investigation failed to show evidence of extraneous infection of any kind. It was felt that the answer lay perhaps in the strain of the seed from which these marrows had grown. Samples of the last marrow were therefore sent to the nurseries

from which the seed had been obtained, but they could throw no light on the problem. A third sample was sent to the county agricultural education department, who asked the public analyst to analyse it. He has kindly allowed me to quote his report, which is as follows :

"Some members of this family of plants are intensely bitter and are used medicinally for this purpose. Occasionally plants do revert and have this very bitter taste. The reason for this instability is obscure and does not appear to be due to soil conditions, as normal fruit and bitter fruit are intermingled. In a similar instance we have shown the bitter principle to be a glucoside. Many of the glucosides are intensely poisonous and would certainly give rise to the symptoms described, although the danger in this case is mitigated by the fact that the taste is so nauseating that it is unlikely anyone would eat any appreciable quantity. Bitter fruits are generally smaller and rougher in appearance compared with normal fruit."

All three marrows in this case appeared normal in size, shape, colour, and consistency.—I am, etc.,

Abingdon, Berks. T. T. BAIRD.

Medicine as a Planned Economy

SIR,—Dr. O. L. Wade (Oct. 16, p. 721) complains that far too much reliance is placed on laboratory tests in diagnosing illness. This may be true of the younger members of hospital staffs, but I do not think it is true of the senior members, who have the tests made to complete the picture, the jig-saw puzzle they strive to put together. The result of the test may prove to be the important piece they have been seeking. For my part, as a pathologist I have always stressed the importance of clinical observation. The fault of the clinician is that he so often does not consult the pathologist about the most suitable test to be undertaken.

If there are too many unnecessary tests demanded by the consultant, this is certainly not true of the general practitioner, whose neglect of helpful pathological investigation is much to be regretted; even the simple tests Dr. Wade lists are asked for far too seldom, to the disadvantage of both doctor and patient.—I am, etc.,

London, W.8. HAROLD H. SANGUINETTI.

H 11 in Malignant Disease

SIR,—The condemnation of H 11 (Oct. 16, pp. 701 and 716) is in my opinion much too sweeping. I have treated seven cases of malignant disease with H 11 and feel that the results justify further use of this extract.

The first case suffered from carcinoma of the cervix which had been treated with radium unsuccessfully and was in a pitiable condition with wasting and pain requiring frequent injections of morphine. Under H 11 the pain steadily improved, appetite returned, and a secondary palpable mass in the pelvis disappeared. She appears to have made a perfect recovery, and is now in excellent health.

The second case was a man with carcinoma of the mamma with multiple secondaries, including one in the humerus, causing gross oedema of the arm with severe pain. He improved for a time. The growth in the humerus became smaller and the oedema very much reduced. His relief was so great that he was indignant that he had not been given H 11 sooner. After three or four months the secondary growths began to increase rapidly; he developed severe toxaemia and died a fortnight later. Although a fatal termination was not prevented the relief of pain and the increased feeling of well-being amply justified the treatment. He also had been previously treated with radium.

The third case suffered from gastric carcinoma with secondaries in the liver, confirmed by laparotomy. Under H 11 his appetite improved, with some gain in weight, and he felt so much better that he intended returning to his business. But after a stormy interview with the man running his business he had a stroke and died suddenly.

The fourth case is a man with an inoperable suprasellar tumour causing progressive loss of sight, severe headaches, and pain in one arm. He is having H 11, and gradually the pain in his arm has gone. The headaches are now not severe enough to bother him, and his sight is slowly improving. Whatever the ultimate result in this case may be, H 11 has proved well worth while for the relief so far obtained.

The fifth case had epithelioma of the jaw with secondary glands in the neck. In this case H 11 did not appear to have any effect and he died after ten weeks' treatment. The sixth case had recurrent carcinoma of the breast after surgical removal. Here again no benefit appeared to follow the use of H 11, and she died.

The seventh case had carcinoma of the cervix and rectum. The pelvis was full of growth, causing retention of urine, and nothing but flatus was being passed from the bowel when she came under my care. H 11 was immediately started, and in two weeks faeces began to be passed and the bladder began to act regularly. Catheterization has not been required since. The abdominal pain she was suffering has all gone, her appetite is moderate, she feels well, but she is not gaining weight and the outlook is very doubtful; but the relief given by H 11 has been great.

All the cases had been seen by experienced surgeons and radiologists, and the correctness of the diagnoses is above question. I feel that there is something in H 11 and regret that it is only in those cases in which surgery and irradiation have failed that one can feel justified in using it at present.—I am, etc.,

Rossall, Lancs. A. H. PENISTAN.

Delayed Diagnosis of Phthisis

SIR,—It was with great interest that I read Dr. Peter Stradling's analysis (Nov. 6, p. 832) on the delays which ensue in the diagnosis of phthisis. There are few chest physicians who will cavil with his general observations and recommendations. Most workers in this field agree that the manifestations of pulmonary tuberculosis are protean in character, and it would therefore be valuable to learn what *precise* criteria the author accepted as being suggestive symptoms (in all his cases) which should have reasonably commended themselves to the attention of the general practitioner. There may be a very real danger otherwise that his analysis scarcely does justice to the harassed and overworked practitioner. Again, it is difficult to appreciate what Dr. Stradling means when he states, "The general practitioner in particular does not at present fully utilize his unique opportunities of *raising the Tuberculosis Service from its present mediocrity* (my italics) to the highly efficient organization that it might and should be." This is a very serious charge that is being levelled against the entire service, and it would be revealing to learn the source and authorship of this information. Is this to be taken as the overall picture of the metropolis, of Willesden, or is this the fruit of Dr. Stradling's experience of the bulk of chest clinics from Land's End to John o' Groats ?

Finally, I must take the author to task when he misinterprets or misquotes a paper of mine which appeared in an issue of this *Journal* (1943, **1**, 283). In this he states that my findings and his were not strictly comparable, as his "refer to a chest clinic; Mann's to a sanatorium." In fact, I gave no indication that such was the case, and they, like his own, were extracted from several chest clinics in the West Riding of Yorkshire. However, the two groups of statistics are for an entirely different reason in no sense comparable. Whereas Dr. Stradling's are those of a clinic in the heart of the metropolis, mine were those of an extensive rural area where indifferent transport facilities and wartime difficulties were no doubt contributory factors in giving a much longer hiatus before the general practitioner was consulted.—I am, etc.,

Halifax, Yorks. BERTRAM MANN.

Self-administered Pneumothorax Refills

SIR,—Dr. Philip Ellman's letter (Oct. 16, p. 723) reminds me that in 1910 my old friend Claude Lillingston gave himself a refill on his arrival in England from Norway. This was the first that had ever been given in England. A week or two later I gave him his next refill, at which time we put together the apparatus named after us.

I am also reminded of a one-time patient of mine whose A.P.T. I started in November, 1913, when he was 28. He was a T.B.-positive case who had been originally slightly ill and in the Mundesley Sanatorium when 21. In 1913 he had signs over the upper half of the left lung and did not improve appreciably after four months' conservative treatment. Recovery proceeded quickly after the A.P.T. I did not see him again for ten years, when he astonished me by telling me that he was continuing to keep his A.P.T. going by self-administered, rather large refills at five-weekly intervals. He was keeping perfectly fit, following his profession, that of an artist, and had not visited a doctor.

In 1934 he wrote me that he was keeping very well and still continuing refills—self-administered—about 250 ml. every five weeks. These he continued for several more years, maintaining excellent health. But later his health broke down, I believe badly and from pulmonary tuberculosis (query in the other lung). I fancy the patient is now dead. The A.P. had been kept up for not less than 25 years. In 1924, when I made a sketch from a screening I did, he had a well-collapsed left lung without displacement of the heart but with some adhesions low down laterally.

One or two more of my ex-patients used to give themselves self-administered refills, and one of these at least was not a doctor. But their cases were not so exceptional as the two I have mentioned above.—I am, etc.,

Mundesley, Norfolk. S. VERE PEARSON.

Breath Sounds in Spontaneous Pneumothorax

SIR,—Recently, while preparing a lecture on spontaneous pneumothorax, I was struck by the inadequacy and inaccuracy of the descriptions of the stethoscopic findings in this condition in the textbooks I had to hand. I think it is important that the attention of students be drawn to these omissions and inexactitudes, because the sound caused by air escaping from the punctured lung into a pneumothorax cavity is one of the most characteristic and easily memorized sounds heard on auscultation, and it is a sound which often enables a confident diagnosis to be made. It is correct to say that this sound has a metallic or amphoric quality. It begins later than the inspiratory breath sound, is often interrupted or cog-wheel in type, and may be heard during inspiration and expiration. It can be so distant and faint that it can easily be overlooked. A similar sound can be produced by sucking air rapidly from an open pneumothorax through an aspiration needle. In a closed pneumothorax this sound is, of course, not heard.

Textbooks describe amphoric breath sounds in a pneumothorax. Amphoric breathing is never heard in a pneumothorax. The sound caused by air escaping into the pleural cavity is not a true breath sound, whereas breath sounds in a closed pneumothorax, if audible, have not an amphoric quality.

Every spontaneous pneumothorax is open at the onset : how long it remains open varies from hours to months, but there is always a stage when the escaping air can be heard if the patient is examined early enough. It is sometimes possible to diagnose a pneumothorax by auscultation in a case where it has never been suspected—e.g., in a case without pain and dyspnoea and without obvious cardiac displacement.—I am, etc.,

Belfast. R. FAWCETT STRONGE.

Resuscitation by Rocking

SIR,—We were interested in the article by Dr. F. C. Eve and the late Dr. N. C. Forsyth (Sept. 18, p. 554) and the reply by Dr. W. N. Leak (Oct. 30, p. 797) regarding the resuscitation of the asphyxiated newborn. For many years we have given nikethamide intracardially to the newborn babe which does not breathe. We use one ampoule of 1.7 ml. "coramine," giving half into the left ventricle and the other half intramuscularly. The dose is split in this way because we find that the whole 1.7 ml. given into the heart causes severe spasm and rigidity of all muscles including those of respiration and thereby defeats its own object.

If the baby does not breathe at once we proceed to mouth-to-mouth insufflation through a layer of gauze. An important practical point is to have a 2-ml. hypodermic syringe and needle, ampoule and file, spirit and swab, ready before the birth of every baby and to make these a routine part of the immediate pre-natal preparations.

We feel that if these measures fail Dr. Eve's mechanical methods should be used, but that the latter should not precede and should not replace the former. Nikethamide and insufflation can be used immediately, they involve no loss of time, and their effect is almost instantaneous, whereas the mechanical methods do need time. Needless to say, nikethamide and insufflation must be used before the heart stops beating.—I am, etc.,

E. LEWIS BUTLER.
SARAH BUTLER.

Birmingham, 23.

Post-gastrectomy Syndrome

SIR,—Your annotation (Sept. 11, p. 524) and articles by others on this subject, in particular that by Dr. W. T. Irvine (p. 514), are of considerable interest and importance. The syndrome is a distressing post-operative complication of what otherwise is a very successful surgical procedure. My own observations based on an experience of thirteen years of the treatment of peptic ulcer and neoplasm of the stomach by partial gastrectomy may be of value.

I have seen a number of cases of the syndrome all presenting similar symptoms varying only in degree. Fullness and discomfort after food, generally accompanied by dizziness, sweating, and a feeling of nausea, are the most common complaints. It is by no means always caused by the taking of a bulky meal but can follow a modest intake of food in many cases. Vomiting, when it occurs, is of two types—an early-morning regurgitation of almost pure bile, which I believe to be due to the loss of the pyloric sphincter control, and vomiting between meals not of actual food but of bile-stained froth.

From a study of my cases certain facts have become apparent:

1. The syndrome appears to be becoming more common. I do not recollect seeing any cases in the follow-up clinic of the late Mr. Cecil Joll prior to the second world war.
2. I have never seen it after gastrectomy for carcinoma.
3. It is less common after gastrectomy for gastric ulcer.
4. It is by no means so common in the older age group of patients—beyond the age of 45.
5. It does not tend to occur while a patient is in hospital, often not appearing until a week or two or even longer after discharge.
6. It is most common after gastrectomy for duodenal ulcer in younger male patients.
7. The type of gastrectomy performed would seem to be of little importance, and I have not seen it as a complication in my very small series of successful total gastrectomies.
8. The majority of the patients in my series were of the introspective type given to excessive worry, and those who have been passed over to my psychiatric colleagues for treatment were said to possess an "inadequate personality."
9. Not a few have responded to ordinary reassurance and sedatives.
10. It would appear to be a self-limiting condition. Most cases have cleared up in a matter of six months after operation whether treated or not. They themselves and what remained of their stomachs appear to have become adjusted to the altered conditions.
11. The more intractable cases have responded well to a course of narcosis and psychotherapy.

My deductions from the above make me believe that there is a strong psychological element as a background to the syndrome (duodenal ulcer itself is held to be a psychosomatic disorder). Coupled with the altered mechanics of the upper intestinal tract brought about by operation, hypoglycaemia certainly is present, but would now appear to be of only secondary importance as a causal factor. Neither can overdistension be blamed, as it is so easily avoided by eating "little and often" rather than taking three bulky meals. There is no truth in the so-called dumping theory, if by such is meant the logging of food in the proximal loop. *X* rays following a barium meal have never revealed such to be the case in my experience. The onset of the syndrome usually coincides with the patient's discharge, when he has to go back to face the world and its vicissitudes once again—that is, when he is removed from the shelter of the hospital and medical attention. The worst thing possible after gastrectomy is to allow the patient to go on thinking that he is still an invalid. All my post-gastrectomy cases are encouraged to return to work as soon as possible, to forget that they ever had indigestion, to eat what they like and to enjoy life, with an injunction to observe all the virtues and in moderation some of the vices.

As to the treatment of the syndrome itself, reassurance and suitable sedation are oftentimes successful, together with adjustment of the intake of food and of meal-times until what remains of the stomach and the proximal jejunum can adequately compensate for the altered conditions. The most intractable cases have been submitted to narcosis and psychotherapy with great success by my colleague, Dr. A. A. Martin, of the Bucks County Mental Hospital, and we hope to publish a series of these cases in the not-far-distant future. I have no personal experience of vagotomy, as I have not yet adopted it as a therapeutic procedure in the treatment of ulcer.

Finally, Dr. F. Lindsay Dickson's letter (Oct. 23, p. 759), in which he enumerates his unfortunate personal experience of

the syndrome and his comments thereon, coincides with my own findings. I trust that his complacency since July 5 (which I, unfortunately, am unable to share) will have completed his cure.—I am, etc.,

Aylesbury, Bucks. RALPH H. GARDINER.

Use and Abuse of Tonsillectomy

SIR,—The whole question of the success or otherwise of the operation for the removal of enlarged tonsils and adenoids depends on a proper selection of cases. After a large number of years as a general practitioner and assistant medical officer of schools I came to the following conclusions :

1. It is one of the most successful operations when performed in suitable cases.
2. It is often performed in unsuitable cases.
3. The habit of bracketing tonsils and adenoids together is a mistake. Enlarged adenoids are infinitely more often the cause of trouble than enlarged tonsils, because they quickly obstruct nasal breathing and give rise to mouth breathing. Enlarged tonsils alone very seldom do this.
4. Tonsils should not be removed just because they are enlarged or because purulent-looking material can be expressed from them. Tonsillectomy should only be performed when there is a history of recurrent attacks of tonsillitis with persistent enlargement of the tonsillar glands of the neck.
5. Adenoids, however, should be removed if causing slight nasal obstruction, deafness, or earache, and should always be followed by deep-breathing exercises through the nose to re-establish nasal breathing. If nasal breathing is not re-established the condition will recur.

I believe that in children the tonsils are part of the mechanism for the manufacture of the antibodies of various infections, particularly streptococcal ones, and should be preserved if carrying out those functions properly. Persistent enlargement of the tonsillar glands is evidence that they have failed and have become a permanent source of infection and should therefore be removed. Selection of cases on the above lines would, I believe, give better results and go a long way to relieve the present shortage of beds.—I am, etc.,

St. Mawes, Cornwall. N. C. PENROSE.

POINTS FROM LETTERS

Partridge Bone in Anal Canal

LIEUT. J. S. HAPPEL, R.A.M.C. (B.A.O.R.), writes: The following case may be of interest and must be rather unusual. The patient was a stout woman, aged 37, who complained of excruciating pain in the anus. Pain dated from three hours earlier, when she had defaecated—a normal motion. Inspection of the anus revealed several small thrombosed external haemorrhoids. The anal sphincter was in extreme spasm, and a finger could not be introduced into the rectum. A presumptive diagnosis of strangulated internal haemorrhoid was made, ¼ gr. (16 mg.) morphine given, and heat applied to the region. Seen eight hours later spasm had subsided considerably, and digital examination of the rectum was carried out. A thin sliver of bone two inches (5.1 cm.) long was found lying obliquely in the rectum, with its proximal end embedded fairly firmly in the posterior wall of the anal canal at the junction of the superficial and deep portions of the sphincter. It was removed without much difficulty. It transpired that the patient had eaten partridge 48 hours before. It is rather astonishing that many feet of bowel should be traversed successfully, only for a hold-up to take place in the last inch and a half.

Breast-feeding

Dr. JAMES S. HALL (Walmer, Kent) writes: Your correspondent Dr. Flora Bridge (Nov. 6, p. 838) ends her plea for breast-feeding by saying that not to persevere with it is "depriving the baby of its surest hold on health." This is an admirable sentiment, but is it really true? I am finding that fewer and fewer mothers are now able to maintain satisfactory breast-feeds, yet their children remain healthy. With more than twenty-five years' experience and four extremely healthy children of my own, all bottle-fed, I cannot determine that artificial feeding has any deterrent effect whatsoever. On the contrary, where there is a bad history of breast-feeding with the first child it is surely better to give the second a flying start with a bottle from birth. To persevere again with the breast is asking for misery for mother, nurse, and child. I am of course open to conviction should sufficient modern evidence be available to the contrary, and I will concede the point that on general grounds in these days of restrictive practices it may be a good thing to make the baby work a little harder for his meals.

Obituary

JOSEPH BLOMFIELD, O.B.E., M.D.

Joseph Blomfield, consulting anaesthetist to St. George's Hospital, died in the West Middlesex Hospital, Isleworth, on Nov. 9, the hospital at which he did his E.M.S. work during the war. He was born in London on March 1, 1870, and was educated at University College School and Cambridge University. He entered St. George's Hospital in 1891, and graduated M.B., B.Ch. in 1894; he proceeded M.D. in 1897. After minor appointments early in his medical career he took up anaesthetics as a specialty, but it was some years before he finally settled down at St. George's. For periods he was anaesthetist to many hospitals, including the Metropolitan, St. Mary's, St. John and St. Elizabeth, the National Dental, and the Grosvenor Hospital for Women and Children. He was senior anaesthetist at St. George's from 1906 until he retired in 1931.

Elliott and Fry

In 1900 he was elected to the select, but small, Society of Anaesthetists, and of this body he became senior secretary in 1905. He was one of the outstanding members of the Society, and it was to a great degree his influence which induced the Society against the strong opposition of many of the older members to form a Section of Anaesthetics at the Royal Society of Medicine. This argument split the old Society of Anaesthetists into two almost equal parts: the members of the Society who were in favour of the proposal became the original members of the Section. Blomfield was one of these, and before many years had passed he became president. He held this office with dignity, being as excellent a president as he always was a chairman of the many societies and committees to which he belonged.

He was a founder of the Association of Anaesthetists, was the first vice-president and the second president, and for a short time after the tragic death of Howard Jones, who was the honorary secretary, he undertook secretarial duties. He was chairman of the Anaesthetists Committee of the Medical Research Council, for which he did yeoman service in dealing with the innumerable new drugs. In the first world war he held a commission in the R.A.M.C. and was attached to St. George's Hospital, which became part of one of the London general hospitals. This entailed very heavy work, but Blomfield found time to give his services at many officers' hospitals, the chief of which was the King Edward VII Hospital, Grosvenor Gardens, where Sister Agnes, a well-known Edwardian figure, was in charge, with whom he became great friends. He was given the O.B.E. in 1919.

For many years Blomfield was a pioneer in anaesthesia, and no anaesthetic group or society was complete without his name. In his younger days he was an able and fluent speaker. He was popular with those colleagues who knew him well enough to appreciate his worth, but he never pushed himself in any way, and he appeared rather retiring and almost shy to those who did not understand him. As an anaesthetist he was one of the old school. He was conservative in outlook and inclined to regard some of the modern innovations as but passing phases, for he had seen many new methods started, forgotten, and then again brought forward as something new.

Some of his best work was done when "avertin" was first introduced into this country; he was chairman of the Anaesthetic Committee of the Medical Research Council at the time. His work at St. George's did much to popularize his method of rectal anaesthesia, which soon became a fashion, if not a craze. Blomfield was the first to point out the limitations of the method and also the danger of using morphine in conjunction with avertin.

He was a good writer, and will be best remembered as such. For years Blomfield was editor of the *British Journal of Anaesthesia* and of the section of anaesthetics in the *Medical Annual*. He was author of a popular book entitled *Anaesthetics*, which ran through many editions. In 1922 he published another book, *Anaesthetics in Practice and Theory*. He wrote many articles in medical journals and in surgical textbooks. He was also author of a history of St. George's Hospital written to commemorate the bicentenary of the hospital.

He was a most regular attendant at the university cricket match at Lord's, and nothing would prevent his annual appearance at this function. In 1945 he was very seriously ill, and, although he made a good recovery, he never regained his full vigour. He still attended many of the meetings of societies, and his presence among the senior members will be much missed. In 1948 he was elected a Fellow of the Faculty of Anaesthetics, Royal College of Surgeons. Without doubt he was a pioneer in anaesthesia, and he has left his mark upon the history and literature of that branch of medicine.—Z. M.

J. P. HELLIWELL, C.B.E., M.R.C.S., L.D.S.

John Percival Helliwell, consulting dental surgeon to the London County Council and formerly Director, Army Dental Service, died on Nov. 7 at the age of 64. He received his professional education at Manchester University and at St. Mary's Hospital, London, and he qualified as a dental surgeon in 1908. In 1910 he was one of the three civilian dentists selected by the War Office to look after the teeth of soldiers serving in India. This was the beginning of the Army Dental Service. He was commissioned in the R.A.M.C. in 1915 when Army dental officers were first admitted to the Corps. He became Inspector of Dental Services at the War Office in 1918, and when the Army Dental Corps was established in 1921 he was chosen to organize it. He believed that dentistry was a branch of medicine, and, feeling the necessity for a medical qualification, he qualified in 1926 at the age of 42. In the same year he was appointed Assistant Director-General, Army Medical Services, with the rank of colonel. He was appointed the first director of the Army Dental Corps in 1935 and was promoted to the rank of major-general—the first dental surgeon to attain this rank. He retired from the Army in 1936 and became consulting dental surgeon to the London County Council, which was then reorganizing its hospital and school dental services. He was an able administrator and organized with great success both Army and civilian dental services. He was chairman of the Army advisory committee on maxillo-facial injuries and a member of the Interdepartmental Committee on Dentistry. He was made a C.B.E. in 1919 and was Colonel Commandant of the Army Dental Corps from 1932 to 1947. He is survived by his widow and a son and daughter.

W. R. Y. writes: With the death of Major-General Helliwell the dental profession has lost one of its most outstanding personalities, and many of his colleagues have lost a true and valued friend. Throughout his professional career he strove consistently for those high ideals which would increase the dignity and appreciation of the dental profession, and the many advances in Service and civil dental organization for which he was responsible will remain a lasting tribute to his memory and to his sound judgment. He expressed pronounced and well-considered views to which he held courageously, sometimes in the face of considerable opposition, and his opponents would readily concede the sincerity and selflessness of his aims and ideals. No one who knew him intimately could escape the kindly influence of his charming and gracious personality, and to many he endeared himself in a measure not often given to those who hold high and responsible office. It was a matter of great concern to his friends that his last two years were clouded with ill-health, but his strength of character and sterling qualities were exemplified in the fortitude and courage with which he withstood his affliction.

Dr. EDWARD PERCY HUGHES DUDLEY died suddenly on Oct. 28 at his home at Caxton, Cambridgeshire, at the age of 74. Dr. Dudley, who was a student at St. Bartholomew's Hospital, qualified in 1904 and joined the late Dr. White in partnership at Caxton in 1908. For 40 years he carried on a scattered rural practice, conducting his own family medical clubs with a simple form of administration suited to his needs and to those of his patients, who were chiefly farmers and their workers. Dr. Dudley had been a keen member of the B.M.A. since 1908, and he was chairman of the Cambridge and Huntingdon Division in 1924–5. He was also for some time a member of the Cambridge Local Medical and Panel Committee. He is survived by his widow and one son and one daughter.

L. B. S. writes: By the tragic death of Dr. E. P. H. Dudley the countryside has lost more than a trusted doctor and familiar figure of the Cambridgeshire by-ways: it is as though one of the last remaining strongholds against the mechanized advance of bureaucratic medicine has fallen. Dr. Dudley enjoyed a high reputation in the county mansions, but it was in the cottage that he was seen at his best. A somewhat diffident manner disguised an inflexible resolution; a profound knowledge of the human animal was combined with a boyish curiosity as to the new, and his car contained in ever-increasing profusion the latest therapeutic agents and instruments of minor surgery. His alacrity to seek assistance was perhaps partly due to a skill in prognosis which amounted almost to instinct, and any little service was repaid a hundredfold. He was kindness itself and never spared himself, carrying on his arduous practice with great courage throughout the war years, and turning, when it was over, to face the appointed day for the National Health Service Act with full knowledge of what it would mean to him and all he represented.

J. M. T. writes: Dr. Dudley succeeded his father-in-law, a bearded majestic figure, who did his rounds on horseback and often combined them with riding to hounds. The motor-cycle and car did little to alter the work except to increase it greatly; especially was this so in wartime. The area of the practice is immense, and it was quite usual for the doctor and his assistant each to do nearly a hundred miles in the day. The writer spent two happy years there and learnt to admire the courage and generosity of a man who, no longer young, always went out no matter what the weather. Even deep snowdrifts would not deter him. Every day was a field-day. There was, first, an unhurried, leisurely preparation of medicines and discussion of cases in the surgery and dispensary, with its open fireplace, the old tap-room of the Crown House, Caxton, where Dick Turpin and his mare Black Bess once lodged. At most three or four patients would attend with forms to be filled in or with requests for visits. Then everything would be packed into the cars; the great doors of the yard would be opened, and off we went, perhaps not to return until 10 at night. Dr. Dudley had a deep sense of the worth of his calling and an amused and shrewd perception of the peculiar social position of the medical practitioner in the country. His greatest pleasure was in good-natured co-operation with his colleagues, and it was to his regret if ever a spirit of rivalry and competition came in to spoil such good relationships. He belonged to a generous age and knew it.

Medico-Legal

FATAL DERMATITIS FROM PYELECTAN

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

A married woman of 47 was admitted to the Minehead and West Somerset Hospital for investigation. She was given an injection of "pyelectan," and developed acute dermatitis and toxaemia from which she died in about two weeks. The pathologist who conducted the necropsy, Dr. Crichton MacGaffey, said that he had found no undoubted evidence of tuberculosis (the patient had recently been treated in a sanatorium); he took it that she had been discharged as cured, and it was a very good cure. The cause of death was first subacute haemorrhagic glomerular nephritis and secondly dermatitis venenata due to the dye. The point was raised that the injection had been given before the report on the urine had come back from the laboratory at Exeter, and he was asked whether it had been reasonable to inject pyelectan before the result of the analysis was known. He answered that this was perhaps a matter of opinion; he himself would have suggested that the microscopical findings should be viewed first of all. There was no urgent necessity to give the injection, but the hospital staff "were out to do a thorough job." They might have been short of time or bed space and have wanted to get it done, but he thought it would have been wiser "to have done the thing one stage at a time." There was no antidote to the dermatitis and it was a very unusual thing

to have happened. He did not think it would happen more easily in a person who had had tuberculosis than in one who had not.

The coroner said he thought the hospital authorities had been acting reasonably in the sense that they wanted to make a thorough investigation. The case had been quite rightly reported to him. He recorded a formal verdict of death by misadventure.

Medical Notes in Parliament

Artificial Limbs

Mr. MARQUAND told Mr. Morley on Nov. 9 that a research unit at Rochampton worked under the direction of the Standing Advisory Committee on Artificial Limbs, of which Sir Charles Darwin was chairman. The second report of the committee, issued in April this year, showed the lines on which research is developing. He circulated in the official report a note on the practical results and the improvements to be expected in the near future. This note ran: *Research work on artificial limbs.*—(1) A number of new arm appliances have been added to the existing list and others are being redesigned and improved. (2) A new artificial arm of improved design has been developed. Six trial orders have been placed, and should these prove satisfactory in all respects the arm will go into general production. (3) A new method of suspension of an artificial leg by suction socket has been developed and is under trial by patients; the trials are most encouraging. (4) A socket of new design for above-knee amputation has been produced and is under trial by over 100 patients. (5) Two new mechanical hands have been submitted by the contractors to the Ministry and are under trial. (6) An apparatus has been designed and is under experimental test for measuring comparatively the thrust which walking imposes on both the artificial and the sound limb. By means of this apparatus it is hoped that much valuable information will be obtained. (7) Work is proceeding on the improvement of crutches, new ideas for which have recently been received by the research department.

Pneumoconiosis

Mr. JAMES GRIFFITHS told Dr. Barnett Stross on Nov. 9 that in 1947, 48 miners in North Staffordshire were certified as suffering from pneumoconiosis as compared with 61 in 1946 and 99 in 1945. He said that although these figures showed a steady reduction it was too early to draw any conclusions from them. The figures include cases of silicosis, as separate figures for silicosis were not available.

Trial of German Field-Marshals

Asked by Mr. WARD on Nov. 9 why his Department's doctors did not accompany the Home Office doctors when they examined the German field-marshals in April, 1948, Mr. SHINWELL said it had been considered that the two examinations should be independent. The Army medical board expressed agreement with the findings of the Home Office doctors on the question of fitness to stand trial.

Mr. NICHOLSON on the same date inquired if the medical officers who visited the German field-marshals in January had any instructions other than to determine whether trial would adversely affect their health.

Mr. SHINWELL replied that the Army medical board was instructed to submit a general report on the health of the officers and an opinion on whether it would adversely affect their health to be tried as war criminals. The board gave a full medical report on the condition of the officers and stated that in its opinion it would adversely affect their health to be tried as war criminals. Later, in April, after the officers had been independently examined by the Home Office medical officers, the Army medical board agreed with the Home Office medical officers that three of the accused were fit to stand trial but that the fourth was not.

Medicines for Private Patients

Sir WAVELL WAKEFIELD on Nov. 11 asked the Minister of Health, in view of his refusal to permit private patients to obtain pharmaceutical services free of charge, to withdraw the pamphlet "The New National Health Service," in which it was stated that any person could use the whole or any part of the Service.

Mr. BEVAN was unwilling to do this. He said people were perfectly free to use any part of the Service, but there must be a limit to the extent to which parts could be subdivided. He would not feel justified in supplying medicines or appliances ordered by doctors who were not taking part in the Service and were under no obligation to observe its rules.

Hearing-aids

Mr. BEVAN announced on Nov. 11 that the following Hearing-Aid Distribution Centres were in operation: Sunderland Royal Infirmary; Cumberland Infirmary, Carlisle; Bradford Royal Ear and Eye Hospital; Royal Sheffield Hospital; Nottingham General Hospital; Norfolk and Norwich Hospital; Royal National Throat, Nose and Ear Hospital, London; King's College Hospital; Metropolitan Ear, Nose and Throat Hospital, London; Radcliffe Infirmary, Oxford; Northampton General Hospital; Prince of Wales Hospital, Plymouth; Bristol Royal Infirmary; Birmingham and Midland Ear and Throat Hospital; North Staffs Royal Infirmary, Stoke-on-Trent; Manchester Hospital for Consumption and Diseases of the Throat and Chest; Queen Victoria Royal Infirmary, Preston; Liverpool Eye, Ear and Throat Infirmary. Additional centres would open in the next few weeks at Hull Royal Infirmary; Addenbrooke's, Cambridge; London Hospital; Kent and Canterbury Hospital, Canterbury; Royal South Hants Hospital, Southampton; Cardiff Royal Infirmary; War Memorial Hospital, Wrexham. There were also a much larger number of hospitals where patients might be examined by otologists before obtaining an aid from one of the above distribution centres.

Claims for Compensation

Sir ERNEST GRAHAM-LITTLE on Nov. 11 asked whether Mr. Bevan knew of the uncertainty among general practitioners about the amount of compensation to which each practitioner would be entitled under the National Health Service Act, 1946, and, as the list of applications had been closed, whether he would give the total number of practitioners between whom the global sum available would be divided, and the total of their claims.

Mr. BEVAN answered that under the National Health Service (Medical Practice Compensation) Regulations, 1948, claims were to be submitted by Oct. 31, but late claims, if there were satisfactory reasons for the delay, could be admitted to April 30, 1949. A final determination of the total amount of compensation would not therefore be possible until after that date. Up to date 13,661 claims had been received from medical practitioners in England and Wales.

School Dentists

Mr. GEORGE TOMLINSON stated on Nov. 11 that a good many school dentists were resigning to set up in practice under the National Health Service. Recruits were not coming forward to fill their place. In consultation with the Minister of Health he was considering the salaries of full-time dentists in the employment of local authorities.

Pensions.—The disability pension payable to a pensioner who suffers from a tropical disease will not necessarily be affected by the fact that pathological tests become negative, since pension is assessed on loss of functional capacity, which may persist after the negative test.

Clean Food.—On Nov. 8 Mr. HARRISON asked the Minister of Food, whether in view of recent prosecutions for preparing food in filthy conditions, he would review his regulations and their enforcement in food-preparation depots. Mr. STRACHEY replied that the conditions under which food was prepared for sale for human consumption were governed by the Food and Drugs Act, 1938, which was enforced by local authorities. Recent cases had not disclosed defects in this Act, but they underlined the importance of rigorous enforcement. Officers of the Ministry of Food had instructions to co-operate to the fullest extent with officers of the local authorities with a view to bringing to justice those who for personal gain disregard the public welfare in this way.

Partnerships.—Mr. BEVAN received on Nov. 8 the Report of the Legal Committee on Medical Partnerships and is considering it.

Unsplinterable Lenses.—Mr. BEVAN is considering whether it is possible to supply unsplinterable lenses under the National Health Service.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

On Oct. 30 the degree of M.D. was conferred on *R. A. D. Crawford, J. N. Milnes, J. S. Heller, and P. D. Samman.

*By proxy.

UNIVERSITY OF GLASGOW

On Nov. 6 the degree of M.D. was conferred on T. McEwan and the degree of Ph.D. on I. C. Michaelson, F.R.F.P.S., D.O.M.S.

UNIVERSITY OF ABERDEEN

At a graduation ceremony held on Oct. 27 the degree of M.D. (with commendation) was conferred on H. McL. Raffan.

UNIVERSITY OF LONDON

Dr. J. W. Trevan, F.R.S., will deliver two lectures on "Statistics from the Standpoint of a Pharmacologist" in the Physiology Theatre of University College, Gower Street, W.C., on Wednesdays, Dec. 1 and 8, at 5.15 p.m. The lectures are open to members of the public without fee or ticket.

The University Court has elected Sir Henry Dale as its Deputy Chairman for 1948–9.

Dr. Charles Reid has resigned the post of Reader in Physiology at London Hospital Medical College, from Sept. 30.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

Mr. A. Dickson Wright will deliver the Dr. John Burns Lecture in the Hall of the Faculty (242, St. Vincent Street, Glasgow) on Wednesday, Nov. 24, at 5 p.m. His subject is "Vascular Surgery." All medical practitioners are invited to attend the lecture.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* the increase of 908 in the notifications of measles was the only rise in the incidence of infectious diseases. There were falls in the incidence of whooping-cough 103, dysentery 31, and diphtheria 24.

The largest rises in the notifications of measles were Lancashire 221, Essex 114, Monmouthshire 107, Derbyshire 104, and Southampton 90; the largest fall was 66 in Lincolnshire. Only small changes occurred in the returns for whooping-cough; the largest were a decrease of 43 in Cornwall and an increase of 32 in Yorkshire West Riding. No large variations were recorded in the local trends of scarlet fever. The largest fluctuations in the returns of diphtheria were a decrease of 10 in Lancashire and a rise of 8 in both London and Essex.

Three more cases of typhoid were notified from the outbreak in Shropshire, Oswestry R.D. The only large return for dysentery was 20 in Lancashire. A fall of 10 in the total notifications of poliomyelitis resulted in the smallest number of notifications since the middle of August. The largest returns of poliomyelitis were London 9, Lancashire 5, Kent 4, Norfolk 4, Yorkshire West Riding 4, and Glamorganshire 4.

In *Scotland* decreases occurred in the notifications of measles 53 and whooping-cough 20, while rises were reported for scarlet fever 43 and diphtheria 24. A small rise in the incidence of diphtheria occurred throughout the country. The increase in cases of scarlet fever was confined to the western area. In Edinburgh a rise of 12 was reported in the number of notifications of dysentery, but elsewhere in the country a slight fall was recorded. An outbreak of paratyphoid fever has been reported from the city of Aberdeen, and up to Nov. 9 there were 11 cases (3 in one family). The origin of the outbreak is at present unknown.

In *Eire* rises were recorded for measles 90, diarrhoea and enteritis 37, and whooping-cough 14; a fall was reported for scarlet fever 20. The notifications of measles in Laoighis, Athy No. 2 R.D., rose from 15 to 71. In Dublin C.B. the notifications of diarrhoea and enteritis increased from 17 to 47.

In *Northern Ireland* a decrease of 59 in the number of cases of measles notified in Belfast C.B. was the chief feature of the returns.

Week Ending November 6

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,471, whooping-cough 2,240, diphtheria 171, measles 6,177, acute pneumonia 496, cerebrospinal fever 21, acute poliomyelitis 73, dysentery 55, paratyphoid 3, and typhoid 4.

No. 44

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Oct. 30.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	(b)	(c)	(d)	(e)	1947 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	22	2	18	1	—	39	—	25	2	—
Deaths		—	—				1	—		
Diphtheria	129	24	53	7	1	178	19	63	12	8
Deaths	2	—	—	—	—	3	—	—	—	—
Dysentery	68	7	63	1	3	126	5	20	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	2	—	1	—	—	—	—	—	—	—
Deaths		—					—			
Erysipelas			44	8	4			29	9	5
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				61					53	
Deaths	32	1	9	4	—	51	3	15	10	8
Measles*	6,211	119	47	127	65	2,052	67	131	207	6
Deaths†			—	—	—	—	—	3	2	—
Ophthalmia neonatorum	45	5	12	1	—	41	3	11	—	—
Deaths										
Paratyphoid fever	7	2	—	1 (B)	—	15	1	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	418	22	4	3	1	502	39	2	2	3
Deaths (from influenza)‡	11	1	1	—	1	16	2	2	—	—
Pneumonia, primary			153	19				215	13	
Deaths	155	19		4	11		32		6	4
Polio-encephalitis, acute	4	1				22	3			
Deaths							1			
Poliomyelitis, acute	66	9	3	3	1	221	20	46	6	4
Deaths§	4	—					—			
Puerperal fever		—	9		—		—	10		—
Deaths										
Puerperal pyrexia‖	107	10	6	—	—	100	4	8	2	3
Deaths		—					—			
Relapsing fever	—	—			—	1	—			—
Deaths										
Scarlet fever	1,374	82	320	169	49	1,529	104	286	73	48
Deaths†			—	—	1	1	—	—	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	10	—	1	1	—	4	—	—	11	—
Deaths	2	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,060	127	75	66	16	1,037	59	41	45	6
Deaths	2	—	—	—	—	4	1	—	1	—
Deaths (0–1 year)	259	30	43	13	13	336	38	64	29	22
Infant mortality rate (per 1,000 live births)										
Deaths (excluding stillbirths)	4,491	723	547	166	118	4,415	739	590	172	118
Annual death rate (per 1,000 persons living)			11·0	10·4				12·3	10·9	
Live births	7,419	1184	870	406	226	7,626	1240	954	364	200
Annual rate per 1,000 persons living			17·6	25·4				19·2	23·0	
Stillbirths	176	27	36			203	34	35		
Rate per 1,000 total births (including stillborn)			40					35		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

Medical News

Birth of a Prince

A son was born to Princess Elizabeth at Buckingham Palace on Nov. 14, and was attended by the following medical men: Sir William Gilliatt, Mr. John H. Peel, Dr. V. F. Hall, Sir John Weir.

Sir William Gilliat, President of the Royal College of Obstetricians and Gynaecologists, received his medical training at the Middlesex Hospital, qualifying in 1908. He obtained the M.B., B.S. (London) in the same year, proceeded M.D. (with gold medal) in 1910, and took the M.S. and F.R.C.S. in 1912. He was elected F.R.C.O.G. in 1929 and President of the Royal College in 1946. The Royal College of Physicians elected him to its Fellowship in 1947. He is Consultant in Obstetrics and Gynaecology at King's College Hospital and an examiner in the University of Cambridge. The knighthood was conferred on him in the Birthday Honours this year.

Mr. Peel qualified at King's College Hospital in 1930 and graduated with the Oxford degree of B.M., B.Ch. in 1932, obtaining the F.R.C.S. a year later. He was elected F.R.C.O.G. in 1944. He is Obstetric and Gynaecological Surgeon at King's College Hospital and the Princess Beatrice Hospital, Consultant Gynaecologist for Puerperal Pyrexia to the Borough of Lambeth, and examiner in the University of London and for the Royal College of Obstetricians and Gynaecologists.

Dr. Hall qualified in 1927 at King's College Hospital, taking the D.A. in 1939; he was elected to the Fellowship of the Faculty of Anaesthetics of the Royal College of Surgeons this year. He is Anaesthetist at King's College Hospital.

Sir John Weir was appointed Physician in Ordinary to the King in 1937. He graduated M.B., Ch.B. at Glasgow University in 1907. In 1932 he was created K.C.V.O. and in 1939 G.C.V.O. Sir John is Consulting Physician to the London Homoeopathic Hospital.

British Council Conference Grants

The British Council has a small fund to enable overseas delegates to attend national or international conferences held in the United Kingdom on scientific subjects, including medicine. Grants are paid to overseas delegates in person and cover subsistence in the United Kingdom for the duration of the conference up to a period of two weeks. Fares to and from the United Kingdom can be paid only in exceptional circumstances. No payment can be made to the convening body to cover their secretarial or other organizing expenses. Grants are made only to delegates who cannot otherwise arrange to come to this country. Conveners of conferences to be held from April 1, 1949, to March 31, 1950, should apply to the Director, Visitors Department, British Council, 3, Hanover Street, W.1, by Jan. 15, 1949, giving particulars of their conference and the number of delegates (and their nationalities) who they think will require assistance. Where it is impossible for conveners to apply by Jan. 15 they may apply later on the understanding that funds may no longer be available. Applications will be considered by the relevant British Council Advisory Panel of scientific experts, and conference conveners will receive a reply by the end of February, 1949.

Commonwealth Fund Fellowships

The Commonwealth Fund of New York has established for British subjects a number of Fellowships tenable in the United States. There are three categories of Fellowships, namely, Ordinary, Home Civil Service, and Overseas Civil Service, and all categories are now open to women. Conditions of appointment and tenure and the emoluments attached to the Fellowships may be obtained from the secretary of the Committee of Award, Commonwealth Fund Fellowships, 35, Portman Square, London, W.1; applications for Fellowships to be awarded in 1949 must reach this address by Feb. 1, 1949.

Guild of St. Luke, SS. Cosmas and Damian

At the annual general meeting of the Guild of St. Luke, SS. Cosmas and Damian, held at the Hospital of St. John and St. Elizabeth on Oct. 31, the following officers were elected for the forthcoming year: *Master*, Dr. W. B. J. Pemberton; *Honorary Secretary*, Dr. W. J. O'Donovan, O.B.E. (130, Harley Street, London, W.1); *Honorary Treasurer*, Dr. P. Corridan (114, Harley Street, London, W.1).

Chief Medical Officer at Colonial Office

Dr. E. D. Pridie has been appointed adviser to the Secretary of State for the Colonies in succession to the late Dr. W. H. Kauntze. The title of the post is now Chief Medical Officer. After serving as Director of Medical Services in the Sudan and in the R.A.M.C. with the Middle East Forces during the war, Dr. Pridie was appointed Health Counsellor to the British Embassy in Egypt in 1945.

Liverpool School of Tropical Medicine

The Liverpool School of Tropical Medicine has been given £10,000 by John Holt and Company (Liverpool) Limited as a birthday gift in honour of the School's inauguration fifty years ago. The generosity of local subscribers and particularly Mr. (later Sir) Alfred Jones, a Liverpool ship-owner, made possible the foundation of the School in 1898. It was formally opened by Lord Lister on April 22, 1899. A special ward was set aside for patients in the Royal Southern Hospital; named the Samuel Henry Thompson Ward, it contained twelve beds and it is recorded (*Journal*, April 29, 1899, p. 1036) that at the opening ceremony the nationalities of the twelve occupants represented China, India, the United States, Norway, Sweden, Russia, Finland, England, and Ireland. Major (later Sir) Ronald Ross was appointed Medical Officer.

Prize for Essay on Colonial Tuberculosis

A prize of 100 guineas will be awarded by the Council of the N.A.P.T. for an essay on "The Control of Tuberculosis in a British Colony." The competition is open to doctors of either sex who are in the service of the Colonial Governments and who are of not more than ten years' or less than five years' medical standing, of which at least three years have been spent overseas in a medical capacity. Competitors should describe their own proposals for a practical scheme for the clinical, social, and administrative control of tuberculosis, either in the British Colonies as a whole or in one or more of them separately. Writers should give their own opinions based on personal experience of public health and anti-tuberculosis work. Essays should be sent to Dr. Harley Williams, Secretary-General, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1, to arrive not later than May 1, 1949. The award of the prize will be notified at the N.A.P.T. Commonwealth and Empire Health and Tuberculosis Conference in London in July, 1949. Essays sent in shall become the property of the N.A.P.T., and any of them may be published at its discretion in the author's name.

The Napier Shaw Premium

The Council of the Institution of Heating and Ventilating Engineers has accepted an offer from Mr. C. G. Vokes, M.I.Mech.E., to provide a sum of money to be used to further the science and art of air conditioning and has decided to establish a fund from which it is proposed to make annual awards during the next few years, to be known as the Napier Shaw Premium. The Council announces that Dr. T. Bedford, D.Sc., Ph.D., Hon. M.I.H.V.E., of the London School of Hygiene and Tropical Medicine, has consented to prepare the first Napier Shaw Premium paper, which it is hoped will be presented at the April, 1949, sessional meeting. The award for 1949 will be made after open competition, and the closing date for submission of papers is March 31, 1949. It is not restricted to members of the Institution. Copies of the regulations will be sent to anyone making application to the secretary, the Institution of Heating and Ventilating Engineers, 75, Eaton Place, London, S.W.1.

COMING EVENTS

Congress of Comparative Pathology

The International Congress of Comparative Pathology will hold its fifth meeting in Istanbul from May 17 to 20, 1949. The Congress covers all aspects of human, plant, and veterinary pathology, and considerable lattitude is permitted in the choice of subjects for discussion. The British National Committee (chairman, Mr. T. Dalling, C.V.O., Ministry of Agriculture) will be glad to receive as soon as possible the titles of communications which members in this country who hope to attend the Congress wish to submit for transmission to the Secrétaire Général of the Permanent Committee. Arrangements for travelling and hotel accommodation are in the hands of Thos. Cook & Son, Ltd. Further information can be obtained from Mr. R. E. Glover (Hon. Sec., British National Committee), Royal Veterinary College, London, N.W.1, or from Pr. N. R. Belger, Taksim, Siraserviler 75/3, Istanbul.

Leeds University Medical School

The annual dinner for past and present students of the Leeds University Medical School will be held at the Great Northern Hotel, Leeds, on Friday, Nov. 26, at 7 for 7.30 p.m., when Dr. J. T. Ingram will preside and the principal speaker will be Lord Moran.

Aberdeen University Club, London

The Aberdeen University Club, London, will hold a reunion supper and dance at Hyde Park Hotel, Knightsbridge, London, S.W., on Friday, Dec. 3, from 7.30 to 11.45 p.m., when Dr. W. A. Milligan will preside. Dinner jackets will be worn, and the price of tickets (including gratuities) is £1 1s. each. All Aberdeen graduates and alumni, whether or not members of the club, will be welcome and may bring guests. Arrangements will be made for non-dancers. Tickets may be had from the secretary, Aberdeen University Club, Southern Hospital, Dartford, Kent, on or before Nov. 26.

SOCIETIES AND LECTURES

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—Nov. 22, 8.30 p.m. "*Gastroscopy.*" Discussion to be introduced by Dr. Avery Jones and Mr. Hermon Taylor.

Tuesday

CHADWICK TRUST.—At Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W., Nov. 23, 2.30 p.m. Bossom Gift Lecture: "*The Influence of Hygiene on the Shape of Buildings,*" by Mr. A. MacDonald.

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh Royal Infirmary (West Medical Lecture Theatre), Nov. 23, 5 p.m., "*Renal Failure,*" by Professor R. Platt.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Nov. 23, 5 p.m. "*Abnormalities of the Cutaneous Circulation in the Lower Limb,*" by Mr. A. K. Monro.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 23, 11 a.m., "*Tabes Dorsalis,*" by Dr. J. C. Hawksley; at St. Peter's Hospital, Henrietta Street, London, W.C., Nov. 23, 5 p.m. "*Retropubic Operations on the Prostate,*" by Mr. A. W. Badenoch.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—Nov. 23, 5 p.m. "*Victorian Medical Administrators and Their Significance for To-day.*" Bradshaw Lecture by Dr. J. A. Charles.

Wednesday

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 24, 11 a.m., "*Syphilis of Skeletal System,*" by Dr. W. N. Mascall; at St. Peter's Hospital, Henrietta Street, London, W.C., Nov. 24, 5 p.m., "*Endoscopic Resection of the Prostate,*" by Mr. R. Ogier Ward.

PLANNING FORUM.—At Planning Centre Hall, 28, King Street, Covent Garden, London, W.C., Nov. 24, 6.15 p.m. "*Work and Health,*" discussion to be opened by Dr. R. S. F. Schilling, Mr. Brian Punch, and Dr. John Burton.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242, St. Vincent Street, Glasgow.—Nov. 24, 5 p.m. "*Vascular Surgery,*" Dr. John Burns Lecture by Mr. A. Dickson Wright.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—Nov. 24, 3.30 p.m. "*The Care and Correction of Dental Defects in Children,*" by Miss Lilah M. Clinch, L.D.S. R.C.S.

WAKEFIELD GENERAL HOSPITAL.—Nov. 24, 8 p.m., Clinical meeting. "*Recent Advances in the Surgical Treatment of Peptic Ulcer,*" by Mr. George Armitage. All practitioners in the area are invited.

Thursday

DEWSBURY: STAINCLIFFE GENERAL HOSPITAL.—Nov. 25, 8 p.m. "*Dysfunctional Uterine Bleeding,*" by Mr. T. N. MacGregor.

EDINBURGH ROYAL INFIRMARY.—Nov. 25, 5 p.m. "*Pneumonia—A Survey—Past and Present,*" Honyman Gillespie Lecture by Dr. Thomas Anderson.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Nov. 25, 11 a.m., "*Relapse, Reinfection, and Super-infection in Syphilis,*" by Dr. W. N. Mascall; at St. Peter's Hospital, Henrietta Street, London, W.C., Nov. 25, 5 p.m., "*Malignant Disease of the Prostate,*" by Mr. J. G. Sandrey.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., Nov. 25, 8.15 p.m. "*The Colchester Taxi Cab Murder (1943),*" by Dr. F. E. Camps.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—Nov. 25, 4.30 p.m. "*Neurology and Psychiatry.*" Lecture-demonstration by Dr. Desmond Curran.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—Nov. 25, 1.15 p.m. "*Posture,*" by Dr. J. T. Aitken.

Friday

KENT PAEDIATRIC SOCIETY.—At Lingfield Epileptic Colony, The Homestead, Lingfield, Surrey, Nov. 26, 2.30 p.m. Meeting, including visit to Special School attached to Colony.

LONDON CHEST HOSPITAL, Victoria Park, E.—Nov. 26, 5 p.m. "*X-ray Kymography of the Heart and Lungs,*" by Dr. Franklin Wood.

LONDON UNIVERSITY.—At Westminster Medical School, Horseferry Road, London, S.W.—Nov. 26, 5.30 p.m. "*Social Factors in Obstetrics.*" Special University Lecture by Professor D. Baird (Edinburgh).

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, London, W.—Nov. 26, 8 p.m. "*The Teaching and Education of the Venereal Diseases,*" discussion to be opened by Dr. Robert Lees.

ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, London, W.C.—Nov. 26, 5.15 p.m. "*Morality and Politics,*" by A. C. Ewing, Litt.D.

ROYAL MEDICAL SOCIETY, 7, Melbourne Place, Edinburgh.—Nov. 26, 8 p.m. "*Patent Ductus Arteriosus,*" by Mr. A. Taylor.

ROYAL PHOTOGRAPHIC SOCIETY OF GREAT BRITAIN: SCIENTIFIC AND TECHNICAL GROUP, 16, Prince's Gate, London, S.W.—Nov. 26, 7 p.m. "*The Reproduction of Radiographs,*" by Messrs. H. S. Tasker and K. H. Gaseltine. Joint meeting with Industrial Radiology Group of Institute of Physics.

SOCIETY OF CHEMICAL INDUSTRY: FINE CHEMICALS GROUP.—At London School of Hygiene and Tropical Medicine, Keppel Street, W.C., Nov. 26, 7 p.m. "*Some Aspects of the Relationship Between Chemical Constitution and Physiological Activity,*" by Dr. F. Bergel, D.Phil. Discussion.

SURREY COUNTY MEDICAL SOCIETY.—At Dorking County Hospital, Nov. 26, 7 p.m. Clinical meeting.

Saturday

ROYAL DENTAL HOSPITAL OF LONDON SCHOOL OF DENTAL SURGERY (University of London).—Nov. 27, Annual clinical "At Home" at the hospital. The annual dinner will be held in the evening at the Savoy Hotel.

APPOINTMENTS

BLAKE, H. ELLIOTT, F.R.C.S., Plastic Surgeon, St. George's Hospital, London, S.W.

DAVIES, IDRIS, M.D., M.R.C.P., D.P.H., Medical Adviser for Wales in connexion with resettlement in employment of men and women disabled through war service or industrial diseases.

GUMLEY, G. A. H., M.D., M.R.C.P.Ed., D.P.H., Group Physician, West Fife Hospitals Group, South-East Regional Hospitals Board for Scotland.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Assistant Medical Registrar to the Gastro-enteritis Flying Squad and Hospital Gastro-enteritis Unit:* J. A. Black, M.B., B.Ch., M.R.C.P. *House-Physicians:* S. J. Macoun, M.B., B.Ch., M.R.C.P., T. R. Savage, B.M., B.Ch., M.R.C.P. *House-Surgeon to Orthopaedic Department:* R. J. Cowan, M.D. *Assistant Resident Medical Officer (Tadworth Court):* Pamela A. Davies, M.B., Ch.B.

HUTCHINSON, W. J., M.B., B.Ch., D.P.H., Deputy Medical Officer of Health, Great Yarmouth.

JOHNSTON, W. R., M.B., B.Ch., D.P.H., Assistant Medical Officer of Health for Londonderry, Northern Ireland.

LESSLIE, ABIGAIL J. M., M.B., Ch.B., D.P.H., Senior Medical Officer for Maternity and Child Welfare in Wolverhampton.

LONDON COUNTY COUNCIL.—*Divisional Medical Officer:* G. O. Mitchell, M.D., M.R.C.P., D.P.H. *Assistant Divisional Medical Officers:* Elsie J. Madeley, M.B., Ch.B., D.P.H., Evelyn C. McD. McGregor, M.B., Ch.B., D.P.H., Evelyn A. M. White, M.R.C.S., L.R.C.P., D.P.H., Violet I. Russell, M.D.

MICHIE, A. McG., M.B., Ch.B., D.P.H., Medical Superintendent for Aberdeen General Hospitals.

OWEN, G. D., M.D., Physician (part-time) to Northallerton Hospitals.

ST. ANDREW'S HOSPITAL, Bow, London, E.—*Senior Resident Anaesthetist:* J. Hamilton, M.B., Ch.B., D.A. *Assistant Medical Officer, Class I:* J. T. Bolger, M.B., B.Ch.

TAYLOR, M., O.B.E., M.D., D.P.H., Medical Officer of Mental Health for the North-East Region, Aberdeen.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Carey.—On Nov. 3, 1948, at Liverpool Maternity Hospital, to Margaret, wife of Dr. A S. Carey, a son—Michael Stuart.

Jackson.—On Nov. 7, 1948, at Middlesex Hospital, London, W., to Lesley (née Bellamy), wife of Mr. Ian Jackson, F.R.C.S., a son—Patrick.

DEATHS

Alexander.—On Nov. 3, 1948, at Bowmont Villa, Kelso, Stuart Maxwell Alexander, M.B., Ch.B.Ed.

Blomfield.—On Nov. 9, 1948, at West Middlesex Hospital, Isleworth, Joseph Blomfield, O.B.E., M.D., aged 78.

Bodger.—On Nov. 3, 1948, at Ridgemount, Astwood Bank, Redditch, Septimus Bodger, M.D., aged 80.

Dalyell.—On Nov. 1, 1948, at Greenwich, Sydney, N.S.W., Elsie Jean Dalyell, O.B.E., M.B.

Deane.—On Nov. 8, 1948, at Meadowland, Old Road, Headington, Oxford, Archibald Deane, M.D.

Dickey.—On Oct. 28, 1948, at Huigra, Ecuador, Herbert Spencer Dickey, M.D., aged 72.

Ferrar.—On Nov. 8, 1948, at 103, Anglesea Road, Dublin, Benjamin Banks Ferrar, M.D., M.R.I.A., formerly Superintendent of the Zoological Gardens, Dublin.

Gillespie.—On Nov. 9, 1948, at Barrowmore, Milnathort, David Gillespie, M.C., M.D., late of 29, Rosslyn Hill, Hampstead, N.W.

Griffiths.—On Nov. 3, 1948, at Derwydd, Cross Hands, Llanelly, Carmarthenshire, David Henry Griffiths, M.R.C.S., L.R.C.P.

Healey.—On Nov. 4, 1948, at Carrobreck, Lower Hellesdon, Frederick Henry Healey, M.D., D.P.M., aged 48.

Hinde.—On Nov. 8, 1948, Francis Richard Berthon Hinde, M.D.Ed.

McGregor.—On Nov. 7, 1948, at 298a, Earl's Court Road, London, S.W., James McGregor, L.R.C.P.&S.Ed. and L.M., late of Portsmouth, aged 89.

McLeman.—Recently, John McLeman, M.B., Ch.B.Ed., of Greenock, Renfrewshire.

Mather.—On Nov. 6, 1948, Norman James Urquhart Mather, M.B., B.Ch., B.A.O.

Spurr.—On Nov. 5, 1948, at 28, Mount Pleasant, Norwich, James Spurr, M.R.C.S., formerly of Lyme Regis and Winchester, aged 90.

Tighe.—Recently, Vincent Paul Tighe, L.R.C.P.&S.I. and L.M., of Dublin.

Williams.—Recently, at Vauxhall House, Llanelly, Carmarthenshire, Sydney Williams, M.R.C.S., L.R.C.P., aged 68.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Lactation in Virgins

Q.—*In her book "Sex and Temperament" (1935, Routledge, p. 193), Margaret Mead, the American ethnologist, describes how one of the savage tribes in New Guinea adopts babies who are then breast-fed by women who have never had children of their own. She claims to have compared two such cases in which adopted children suckled by mothers in whom lactation had been artificially stimulated grew just as well as their twin brothers or sisters. This observation, if correct, would seem to contradict all our knowledge of lactation. What is the explanation?*

A.—The occurrence of lactation in virgins has been described from time to time, and several cases are mentioned by D. C. L. Fitzwilliams in his book *On the Breast* (1924, London, Heinemann). In all these cases lactation was induced by suckling, and the phenomenon is recorded even at 8 years of age (in a virgin negress). He also notes similar occurrences in men and in extremely aged parous women. Full details are not given, but there is nothing to suggest that these individuals had any disease of the pituitary or other endocrine organs. Our present knowledge of the physiology of lactation is not so complete as to rule out the possibility of the events described in the question. Indeed, the more that is learned of this function and its control, the more complicated it becomes. Although it is fairly well established that the onset of lactation in the human being is brought about by a hormone of the anterior pituitary acting on breasts already primed by oestrogens and progesterone (and possibly by other anterior pituitary factors), it also seems clear that the maintenance of lactation is essentially the result of suckling. There is some difference of opinion about the mechanism whereby suckling acts. Some believe that it is purely local, that the regular emptying of the breasts favours further secretion; others consider that there is a nervous reflex and that suckling stimulates the anterior pituitary to release more prolactin, and also that it stimulates the posterior pituitary to liberate a factor which causes contraction of the muscular tissue around the lacteal ducts. Emotional factors also possibly play a part, and a well-developed maternal solicitude for the child may influence the lactogenic function of the pituitary. If the latter views are correct, it seems feasible that, in certain susceptible women with an overwhelming desire to look after a newborn child, regular suckling might prove a sufficient stimulus to the pituitary to initiate lactation.

Faecal Incontinence in the Aged

Q.—*What is the treatment for lack of control of the sphincter ani in old people without any obvious local cause?*

A.—Both urinary and faecal incontinence are common penalties of old age. Some interesting observations by Wilson (*Lancet*, 1948, 2, 374) have recently shown the former to depend largely on an overactivity of the neuromuscular mechanism of the bladder. He found that weakness of the sphincter was a rare cause. In some the disturbance depended on local irritative factors, and the common reason was loss of cortical control. The bladder and the rectum are so similar in function that it seems probable that his observations can be applied to the faecal incontinence of the aged, although general experience suggests that loss of tone of the sphincter is likely to play a more important part in the latter. Treatment is not satisfactory. Improvement will normally follow measures to inculcate the regular bowel habits from which frequently the patient has lapsed. It is wise to avoid purgation and to ensure a well-formed stool by means of a diet containing adequate roughage. The aim is to secure a complete evacuation at a fixed hour each day, and the patient should be instructed to go to stool after breakfast even in the absence of the normal urge. If there is no spontaneous evacuation resort must be made to enemata, which have the effect of re-educating the bowel. Impaction of faeces in the rectum is a cause of apparent incontinence and may demand digital evacuation.

Rubella in Pregnancy

Q.—*Are any statistics available regarding the incidence of blindness, partial or complete, in the newborn infant of a mother infected with rubella? What is the pathology of the condition?*

A.—It is generally accepted now that an attack of rubella in the mother during the early months of pregnancy leads to ocular and other congenital anomalies in the offspring. The frequency of these occurrences has not been established, and it is obviously impossible that they should be until a large number of expectant mothers with rubella have been followed up systematically. As the time factor is important (rubella late in pregnancy appears to be harmless) the difficulty in giving statistics is still further increased. In general terms, it is probably correct to say that rubella in the mother is of little significance for pregnancy as a whole. It is of considerable significance in the second and third months of pregnancy, and it is possible that an attack of rubella even before conception may also be of importance, as the persistence of the virus after the acute attack has passed off may still influence the developing embryo. Whether rubella in the early months of pregnancy must inevitably lead to congenital malformations in the offspring is not known; such evidence as is available suggests that they are the exception rather than the rule. It is known from experimental embryology that disturbances in the chemical and physical environment of a growing embryo have serious results and may lead to the death of the embryo. It is presumed that the mechanism in rubella is the passage of the virus through the placenta (which normally acts as a barrier against most noxious agents) so that the embryo is exposed to the action of this virus. When organs are fully formed the effects are slight, or there may be none at all. With organs still in the stage of active formation the outcome may be disastrous. This conforms to the findings in experimental embryology that the effect of noxious agents is more pronounced during the early stages of development than later.

Calciferol in Hilar Adenitis

Q.—*It is believed that calciferol in daily doses of 100,000 to 150,000 units produces shrinkage and calcification in tuberculous cervical adenitis; can the same be said for the enlarged hilar glands in primary tuberculosis? If so, is calciferol to be recommended? Can safety in its use be presumed when careful clinical observation is maintained and the administration promptly stopped on the appearance of any indication of toxicity? Can any therapeutic effect be expected where the dosage is well below the tolerated maximum?*

A.—Whereas there is no doubt of the value of calciferol in cutaneous tuberculosis, its effectiveness in other forms of the disease has not yet been fully estimated. However, there have been encouraging reports of its use for glandular lesions. There would appear to be no contraindication to the use of this drug in tuberculous hilar adenitis provided proper precautions are observed. Judging by experience in the treatment of cutaneous tuberculosis, it is most unlikely that small doses would be of any value.

Toxic Effects of Amphetamine

Q.—*In prescribing amphetamine for chronic states of depression in a woman of 40 are there any toxic effects of a prohibitive nature that might develop on prolonged administration—say four months? Over such a relatively long period has the drug any permanent effects on the central nervous system which would lower the mental capacity for, say, shorthand-typing?*

A.—Prolonged administration of amphetamine in the patient described may be accompanied by (1) a growing feeling of irritability and nervousness; (2) aggravation of sleeplessness, if this is present; (3) increased depression as the effect of each dose wears off; and (4) a liability to fainting attacks. There will be a loss of appetite, which will be a good thing if the

patient is obese but bad if she is thin. None of these effects are reasons against trying this drug, but a watch must be kept on the patient. There is no evidence that amphetamine produces permanent effects on the central nervous system or any lowering of mental capacity.

Residual Pelvic Abscess

Q.—*About a year ago a woman of 35 was operated on for a perforated appendix; she developed a pelvic abscess a week later which burst into the rectum. After a long convalescence she is now fairly fit, but still has occasional looseness of the bowels, with discharge of pus. She was recently free from symptoms for a whole week. Is the condition likely to recover spontaneously? Is radiological investigation by barium enema free from risk? Is further surgery necessary?*

A.—A pelvic abscess discharging spontaneously into the rectum should heal automatically within a few weeks. The year that has elapsed in this case would seem to make some investigation imperative, and a barium enema should be perfectly safe. Presumably the residual abscess cavity is completely walled off by fibrous tissue. This same fact indicates the line of treatment, which should be a wider opening of the residual cavity into the rectum if the region concerned is reasonably accessible. It might be presumed that failure of resolution has been due to inadequate natural drainage and that possibly further and more adequate opening of the existing communication with the bowel may achieve the required result.

Persistent Nasal Catarrh

Q.—*For the past year a child of 6 has had moderate nasal catarrh, shown by "snorting" at intervals and by mucus being blown from one nostril perhaps two or three times a day. The child mouth-breathes by day but sleeps with the mouth closed, and there is no snoring or cough. What treatment should be given and, particularly, is adenoidectomy advisable?*

A.—The symptoms suggest chronic sinusitis, probably associated with adenoids; but it should be possible to make a definite diagnosis by skiagrams and by mirror examination of the nasopharynx. If there is sinusitis only, instillation of 0.5% solution of ephedrine in normal saline night and morning should suffice. If adenoids are present or suspected they should be removed and the antra punctured and washed out under short general anaesthesia.

Vitamin K and Menstruation

Q.—*An unmarried woman aged 37 took normal doses of vitamin K last winter for chilblains. It proved highly successful, and she is anxious to take it again this winter. Since January, however, she has had only one menstrual period—in April. There is no other apparent cause for the amenorrhoea. Is there likely to be any connexion between the vitamin K and the amenorrhoea, and, if so, is this a contraindication to its use?*

A.—In the doses in which vitamin K is used it has no effect whatsoever on the menstrual cycle. In fact large doses have been given experimentally to suppress menstruation and to treat menorrhagia, but without effect.

Treatment of Peripheral Vascular Disease

Q.—*A male aged 76 suffers from severe pain in his left leg due to atheroma of the arteries. He has no pain when in bed, but suffers acutely when sitting or walking. On rising from a chair he has to stand for a few moments before he can move. Apart from the local condition, his general health is excellent and his heart sound. Can you suggest any drug which I could prescribe?*

A.—It is not common for peripheral vascular disease to cause pain when sitting in a chair, but not when lying, unless erythromelalgia—in which pain is aggravated when the limb is dependent—is present. The medicinal treatment is twofold: by means of simple analgesics and by reputed vasodilators. The effect of the drugs of the second group is unpredictable; although usually disappointing, they should always be given a trial. Papaverine hydrochloride ½ to 1 gr. (32 to 65 mg.) subcutaneously or by mouth, acetyl-β-methylcholine 0.1 to 0.5 g. orally, theobromine sodium salicylate 10 to 15 gr. (0.65 to 1 g.), and nicotinic acid 50 mg. have all been recommended and may be used in these doses three to four times daily. Dried thyroid is sometimes useful. More patients are helped, perhaps, by physical methods such as intermittent venous occlusion.

NOTES AND COMMENTS

Lactating Baby.—Dr. J. C. VALENTINE (Lecturer in Pathology in the University of Bristol) writes: In reply to a question regarding the treatment of lactation in an infant (Oct. 23, p. 768) you suggest the administration of testosterone. While on theoretical grounds this might be of value—since it is known to be effective in inhibiting milk secretion in women—there is some evidence that it may not be effective in the newborn infant. Slobozianu[1] injected testosterone intramuscularly into male and female newborn infants and found that the incidence of enlargement and milk secretion was thereby increased. He did, however, find that with large doses there was some inhibition of milk secretion, but even with 25 mg. doses 12% of the boys secreted milk.

Another method commonly used to inhibit lactation in women is the administration of oestrogens, natural or synthetic. Dr. Margaret Robinson[2] has found that in the newborn the application to the breasts of lint soaked in a 5% solution of stilboestrol in arachis oil, followed by gentle expression of the milk, soon relieves the engorgement. On the other hand Slobozianu injected oestrone intramuscularly into newborn infants and found that this resulted in an increased incidence of mammary enlargement and milk secretion. It would be of interest to know the effect of oral or parenteral administration of stilboestrol. There is additional support for Slobozianu's work in the papers of Abraham[3] and Dobszay.[4] Abraham found that by the injection of oestrin he was able to cause mammary enlargement and secretion in the newborn to return after they had ceased; and Dobszay was able to induce mammary enlargement in the newborn by the injection of oestrin, and then, by the injection of pituitary mammotropic hormone, was able to induce colostrum secretion.

REFERENCES

1 *Schweiz. med. Wschr.*, 1946, **76**, 203.
2 *Brit. med. Bull.*, 1947, **5**, 164.
3 *Med. Klinik*, 1930, **26**, 164.
4 *Dtsch. med. Wschr.*, 1935, **61**, 1314.

Calcium Iodide for Cataract.—Mr. SYDNEY TIBBLES (London, W.1) writes: In "Any Questions?" (Oct. 2, p. 667) the question and answer given were pretty much the same as those to which I gave a fairly full explanation of my own experience in the *Journal* of Sept. 6, 1947 (p. 404). This provoked no protests but produced many medical men with cataract, one of whom was a well-known eye surgeon, while another, in the late forties, put the commencement of his troubles down to convulsive treatment given for some mental breakdown. In thirty-odd years of using iodides for early lens changes I can only think of four that had to be operated on in the end, and many of my cases have attended and have come back regularly, some for as long as twenty-five years. Two patients with early changes in both eyes have, as test cases, been told to use the treatment for one eye only for the past four or five years, but in each case the eye that had no treatment became worse than its fellow. In the end treatment was commenced for the second eye. This iodide treatment does not profess to cure cataract, but apparently in a very large number of early cases the degenerative changes can be controlled for a large number of years. Before July 5, 1948, a very much larger number of cataract patients in an advanced stage were seen in hospital as compared with private practice. Patients who have to travel a long way to hospital, wasting half a day off from work, often put off their troubles till one eye is blind and the other beginning to fail before they seek advice. The great advantage of eye clinics, such as those sponsored by the B.M.A. (National Eye Service prior to the new N.H.S. scheme), was that the patient could make an appointment to suit himself and seek advice somewhere near where he lived.

Correction.—Mr. E. W. RICHES (London, W.1) points out that in our report of the meeting of the Medical Society of London held on Oct. 25 (Nov. 6, p. 831) it was wrongly stated that he spoke on the use of streptomycin in tuberculous infections of the urinary tract. His paper was concerned with non-tuberculous infections.

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